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STORAGE

THE NERVOUS AFFECTIONS OF THE HEART.*

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The Harvey Society has been founded for the purpose of forming a connecting link between the scientific research work of the laboratories and medical practice. I am greatly indebted to your president for his kind invitation to deliver a lecture before your society.

It is my intention to address you to-night on the nervous diseases of the heart. It may be asked whether this is a problem sufficiently scientific to conform fully with the purpose of this society. I hope it is. As a professor of clinical medicine I hold the opinion that an observation made at the bedside is as well to be considered scientific as an observation made on an animal; nor do I think that, because it is unable to speak, the rabbit is a more scientific animal than man.

I have selected this subject because it illustrates better than many others that our clinical conceptions are founded on experimental physiology. It is not long since we first ventured, and then only with some hesitation, to apply conclusions drawn from laboratory experiments to the pathology of the human heart. Now, since Deneke's successful experiments on the human heart, we see our analogies in a clearer light. Deneke isolated the heart of a criminal immediately after execution, and by perfusing it with Ringer's solution and then with blood, found that it beat regularly for a considerable length of time and obeyed the same general laws that apply to the heart of the dog and rabbit.

Before we can comprehend the nervous *pathology* of the heart, we have to ask what rôle the nervous system plays in the *normal* movements, not only of the heart, but of the blood vessels as well, for we must realize at the start that we can never look on the heart as a separate entity, but that the heart of the higher as well as of the lower animals is only a part of the whole circulatory system, and that it stands in closest relationship with the blood vessels.

We know now that the heart removed from the thorax and cut off from all its connections with the cerebrospinal and the sympathetic nervous system pulsates regularly. Therefore, we draw the conclusion that the nerves running to the heart never originate the heart movements,

* Harvey Lecture, delivered at the New York Academy of Medicine, March 9, 1907.

although they may influence them, interfere with, and even stop them. The origin of the pulsations lies in the heart itself and it is the flow of the blood through the heart, and especially through its own arteries, which not only acts as a nutrient, but also affords the stimulus. The same stimulus can be produced also by Ringer's solution, and Howell of Baltimore has proved that the calcium ions especially are of importance.

To this *constant* stimulus the heart answers with *rhythmic* contractions quite in the same manner as the stomach, the intestines and the ureters respond with rhythmic peristalsis to the constant stimulus of their contents. The stimulus acts on the muscle of the heart, but it is not yet clear whether it is on the muscle fiber itself that the stimulus first acts, or whether the fine network of intrinsic nerves takes up the stimulus and transfers the irritation to the muscle fibrils. While Engelmann and the Leipzig school adhere to the muscular hypothesis, Bethe and recently Hering strongly defend the nervous origin of the irritation.

The irritability of the heart muscle ceases during and immediately after the systolic contraction and returns gradually during the diastolic pause until it reaches a point sufficient to respond again with a new contraction to the continued stimulus of the blood flow.

This refractory period may be shortened, as is the case in paroxysmal tachycardia, or it may be of longer duration when the irritability of the heart muscle is impaired by pathologic processes.

Every part of the heart is irritable, and every part answers to the normal stimulus with its own rhythm, but the irritability is developed in the highest degree in the venous part of the right auricle, and this most easily excitable part, whose own pulsations are more frequent than those of the ventricles, takes the lead of the other parts and determines the rate of their pulsations. So the venous part of the auricle forces its rhythm on the other parts of the auricles and on the ventricles with which it is connected.

The impulse from the auricles to the ventricles goes through the bundle of His. We have learned its nature and course only within the last year, when Tawara published his studies on the heart of different animals. In the human heart the shape and distribution of the His bundle seems to be less simple than in dogs, sheep and calves, and is not yet fully known. In the lower animals His' bundle arises in the form of a knot in the septum auriculorum, passes immediately in front of the septum pellucidum to the muscular wall between the right and left ventricle, divides into two branches, either of which runs as a closed bundle to the apex of each ventricle and divides there into fine filaments supplying the papillary muscles and all the other parts of the ventricular

walls. This bundle consists of peculiar shaped muscle cells first described by Purkinje. The transmission of the impulse from the auricles to the ventricles occurs with a definite delay, and it seems that the peculiar construction of the Purkinje muscle gives an explanation for this delay.

Both ventricles act synchronously and, indeed, this exact synchronism remains intact for as long a time as the two ventricles are connected by their muscle bundles. Hering concludes from his experiments on animals that a separate contraction of a single ventricle never occurs, and that the old clinical conception of hemisystolia was erroneous. When we consider that the muscle bundles of the right ventricle overlap to a considerable extent the central muscle nucleus of the left ventricle, and are closely mingled with it, this view looks very reasonable. But Kraus and Nicolai, in their latest experiments, conclude from the electrocardiogram of the human heart that in some cases of irregularity a dissociation between the contraction of the right and left ventricle does take place.

When the conducting path between auricles and ventricles becomes impaired the delay between the auricular and ventricular contractions will be longer, or some of the ventricular contractions may fall out altogether, so that, as Erlanger has demonstrated, not every auricular contraction is followed by a ventricular one. Not only anatomic lesions of the His bundle, but also some poisons (digitalis) and nervous influences increase this delay and, therefore, are able to produce omissions of single ventricular contractions.

If the His bundle is completely cut across, the ventricles do not remain permanently at rest; after a short stop they again begin to pulsate, but in their own rhythm, which is totally independent of the auricular movements and is characterized by its slow rate—thirty to twelve beats per minute. This is the case in the Adams-Stokes symptom-complex of paroxysmal bradycardia, and this disease is, therefore, not to be considered as a nervous one. In a very marked case of paroxysmal bradycardia, which has been studied in my clinic, we found at the autopsy a large white scar on both sides of the septum ventriculorum exactly at the site of the His bundle; similar observations have been reported by others. It is not yet clear why in such cases of severe anatomic lesions and destructions of the His bundle a permanent dissociation and a constant bradycardia does not take place, and why in such cases periods of complete dissociation commonly alternate with periods of two, three or four auricular contractions to one ventricular contraction, and sometimes with periods of one to one, viz., those of normal type.

If any part of the heart muscle is struck by an extra stimulus in

addition to the normal one, it can respond with an extra contraction or a premature systole, which interferes with the normal rhythm. The extra systoles are, according to our observations, commonly of a shorter duration, and they are of lesser intensity the sooner they follow after the end of the preceding normal contraction. The extra systolic contractions may start from the auricles or from either ventricle, and they are the commonest source of irregularity. In the human heart we observe these extrasystoles especially when the muscle has to struggle against an abnormal high blood pressure and against a condition of congestion, or when the heart muscle has become abnormally irritable. This is the case in many myocardial affections. We may say, therefore, that extrasystolic irregularities manifest themselves especially when the mechanical power of the heart is in disproportion to the opposing forces.

We have seen that the cardiac muscle is an automatic apparatus. Yet this apparatus works under the permanent control and influence of the central nervous system.

The nerves which run to the heart influence the frequency of contractions, their type and strength; they also increase or diminish the myocardial irritability and the transmission of the stimulus from one part to the other. We shall never be able to find our way through the inextricable network of nerve plexuses running to the heart and surrounding it, but we know something about the functions of the vagus and of the sympathetic nerves. The inhibitory influence of the vagus seems to be of greater importance than the augmentatory one of the sympathetic. The vagus nerve arises in that important region of the medulla oblongata where we find also the centers for respiratory movements and of the vasomotor system, and we are sure that these centers are in closest connection to each other.

The vagus sends fibers especially to the venous part of the auricles, and these particular fibers alone exert a chronotropic influence, that is, they affect the frequency of the heart contractions. Other parts of the vagus run to the septum auriculorum and ventriculorum and have an inhibitory action on the irritability and the energy of the muscular contractions, as well as on the conducting functions of the His bundle.

The vagus passes to the heart as white, medullated fibers. These do not end in the muscular fibers directly, like the motor nerves of the voluntary muscles, but seem to end exclusively in ganglionic cells, from whence non-medullated, gray fibers issue. The vagus is, therefore, to be considered merely as a preganglionic nerve, and we must realize that there is no essential difference between the vagus and the white rami communicantes of the spinal cord going to the sympathetic ganglia.

Both pass as white fibers from the central nervous system to sympathetic ganglion cells and both innervate involuntary movements.

Besides these centrifugal nerve bundles, the vagus has also a centripetal part, the so-called depressor nerve. This is not so much the sensory nerve of the heart itself as of the aorta, and it runs to the centers in the medulla oblongata. If the pressure in the aorta becomes too high, an impulse is carried through the depressor nerve to the vagus and vasomotor centers and produces an inhibitory reflex on the heart and a lowering of the blood pressure.

Summarizing, we can say the vagus reduces the work of the heart to that degree which is sufficient for the momentary exigencies of the circulation. The vagus is set in action by the heart itself or by the aorta whenever a protection for the heart is needed, and it is set in action by other organs, whenever a diminution of the blood supply is wanted.

On the other hand, the accelerans of the sympathetic system stimulates the heart to a greater effort and to a more frequent action for the benefit of other organs, for instance, of the working muscle. Every strong exertion of the voluntary muscles raises the frequency and the effort of the heart by way of the sympathetic nerves.

The sympathetic accelerator nerves leave the spinal cord at the level of the first of the fifth dorsal segment in the form of white, medullated, rami communicantes. They issue with the anterior roots and run to the ganglion stellatum and ganglion cervicale inferior. The postganglionic gray fibers arise from these ganglia and run to the various parts of the heart. Some of the sympathetic fibers pass to the venous parts of the auricles, and it is plausible to believe that these only have an increasing effect on the cardiac frequency. Other fibers of the sympathetic go to the ventricular muscle and increase the force of contraction, the irritability and conductivity, and shorten the duration of the systole.

It has been in doubt for a long time whether the sympathetic carries any centripetal, that is, sensory fibers. The embryologic origin of the sympathetic nerves and ganglia from the posterior spinal roots and the intervertebral ganglia seems to prove that there are indeed sensory functions in the sympathetic system, and many experimental and clinical observations also speak in favor of this belief. These sensory fibers of the sympathetic carry impulses of which we ordinarily are not conscious, and which are involved in the manifold unconscious sympathetic reflexes. The well-known fact that in angina pectoris a distinct pain is felt in the region of the lower cervical or the uppermost dorsal

spinal segments, and that often an area of hyperesthesia can be detected in parts of the arm and chest receiving their nerve supply from the same spinal segments (Head) leads to the conclusion that sensory fibers run from the heart to these segments of the spinal cord, for, as far as we know, there are no other paths for these sensory fibers except in the sympathetic system. Hence this clinical observation speaks in favor of the supposition of centripetal sympathetic fibers.

The double innervation of the heart through inhibitory and augmentatory nerves corresponds entirely to the innervation of all the other organs containing involuntary muscle, the stomach, the intestines (where we again see the vagus as an antagonist of the sympathetic), the bladder, but particularly the blood vessels. The blood vessels, and especially the finest arteries, are, like the heart, under the influence of inhibitory (dilatator) and augmentatory (constrictor) fibers. Indeed we can say that the accelerator (augmentatory) cardiac nerves are simply a part of the general vasoconstrictor sympathetic nervous system.

The vasoconstrictor nerves leave the spinal cord in the anterior roots in the form of white rami going to the sympathetic ganglia, from the dorsal to the third lumbar segments, the splanchnics belonging to these preganglionic white fibers. It will be remembered that the vasodilator nerves arise with the cerebral nerves, such as the vagus, and with the posterior roots of the spinal cord, from the uppermost cervical to the sacral segments.

Besides this central nervous influence on the caliber of the blood vessels we must suppose also certain local automatic contractions and dilatations of the finest arteries and capillaries which continue their action when all nerve supply has been cut off. The researches of Stricker and of others of recent times seem to prove that the automatic action of the capillaries plays an important part in the circulation of the blood and lymph. Be this as it may, it is certain that the vasomotor nerves have a very powerful influence on one of the most important and incomprehensible regulatory mechanisms, viz., the maintenance of the normal blood pressure, a regulatory mechanism whose importance stands in no respect below that of the maintenance of the body temperature.

This whole regulatory mechanism of the heart and vessels works under the control of the central nervous system, especially the brain; it responds to every incident in the life of the body, to psychic excitement, joy, fear and depression, to attentiveness, mood and fatigue; every muscular exertion, all changes of temperature act on it, and through it on the heart and vessels and blood pressure.

The morbid results of many cardiac diseases, of myodegenerations of

mitral or aortic stenosis, find a compensation in vasomotor contractions. On the other hand, we see that temporary or lasting changes in the blood vessels find a compensation through an increase or a diminution of the heart work.

Now that we have reviewed some general conceptions of the part played by the nervous system in the entire circulatory apparatus, let us consider in what form disturbances of the nervous system manifest themselves on the circulation.

Cardiac symptoms may sometimes arise from coarse anatomic lesions of the central nervous system or the vagus. Cases have been reported in which paroxysmal tachycardia was the consequence of a syphilitic disease of the basis cerebri and the oblongata, and severe compression of the vagus trunk is said to have provoked attacks of bradycardia and even of momentary stoppage of the cardiac beat, but it is not yet known whether we may regard some cases of the Adams-Stokes disease as a consequence of a damage done to the vagus or whether all such cases belong to alterations of the His bundle.

Far more frequently than with organic lesions of the nervous system do we see cardiac and vasomotor symptoms in connection with a general and *functional* nervous disease, especially with neurasthenia. In neurasthenia the irritable weakness and instability are not confined to the mind and the cerebral functions alone, but often involve a debility of the peripheral nerves also. Along with neurasthenia proper we must maintain with Möbius the old conception of nervousness. Nervousness is characterized by an over-irritability of the mind and the central nervous system. Irritation of one center irradiates farther and draws into play more centers than normally; therefore, all reflex functions are exaggerated. With nervous individuals disorders of the circulatory system play a very important part, and, indeed, a great many symptoms of neurasthenia and nervousness find an explanation in local or general disturbances of the heart and the vasomotor system.

Among the symptoms of the nervous heart we have first to consider *alterations in the rate of pulsations.* We note that usually the frequency of pulsations is increased and often to a high degree. But the increase is seldom a permanent one. A permanent acceleration points rather to other cardiac diseases. It is far more common, and very characteristic of nervous disturbances, to see periods of rapid pulse alternate with a normal rate or even with periods of bradycardia. Indeed the patient who has attracted our attention during the consultation because of his stormy, excited and frequent cardiac action, complains often less of the tachycardia than of the slow heart rate which he has observed in the

morning after sleep or during rest and which, if he anxiously palpates his pulse, gives him the hypochondriacal impression of cardiac weakness.

In short, the nervous heart reacts with an excessive alteration of frequency to all those conditions which produce in the healthy individual only a moderate increase of the pulse rate, for example, to the digestion of food, to coffee and alcoholic drinks (intolerance against alcohol) to every kind of muscular exertion, but above all to psychic impressions. It is characteristic that the increase in frequency is far more marked during psychic disturbances (as called forth, for instance, by fear of the doctor) than during muscular work. Muscular work provokes in the nervous heart an acceleration of the pulse rate, but not the symptoms of defective circulation or breathlessness.

Once a young physician, climbing up a steep hill in company with an experienced physician, described to him in rapid conversation his cardiac troubles and palpitations. The older physician replied: "You have a nervous heart and no organic cardiac trouble, else during climbing you would not continue to talk but rather would gasp for breath."

Besides this discrepancy between the high pulse rate and the subjective symptom of palpitation on the one hand, and the absence of symptoms of defective circulation on the other, it is very characteristic that the increased frequency due to muscular work diminishes when work continues and gives way to a normal rate in a few minutes after the muscular exertion has ceased. In organic cardiac failure, as in myocardial weakness, we see that muscular strain provokes also a high pulse frequency, but in addition shortness of breath, cyanosis, sinking of the blood pressure and every symptom of defective circulation, while after the cessation of the exercise a much longer period elapses before the normal pulse rate and respiration is restored.

In closest relationship to pulse rate stands the question of *rhythm*. Does arrhythmia really occur in the nervous heart? It does, but not to any such extent as is generally believed. The only form of arrhythmia whose connection with nervousness we are sure of is the so-called respiratory or infantile arhythmia. Because neither of these names is fully explanatory I propose the name of "changing pulse rate." We understand by this designation a pulse in which periods of more frequent action alternate quickly with periods of lesser frequency, the variations concerning only the duration of the diastole, while the systole and the relation between the action of auricles and ventricles remain unaltered. In healthy people, and especially in children, forced inspiration and expiration produce a slight but distinct increase and decrease of pulse rate. These periodic changes of frequency are developed to a much higher de-

gree in nervous individuals, and it is clear that this changing pulse is nothing else than an exaggeration of a normal reflex, of a reflex whose path and nature are well known, for we are sure it goes over the vagus, and is to be considered a sign of an unstable equilibrium of the vagus center. This symptom belongs to the same series as the exaggeration of the vasomotor reflexes, or of the knee-jerk, so commonly found in nervous individuals. And since such a respiratory irregularity is never observed in organic cardiac diseases, this symptom is of no little diagnostic value.

Regarding the other forms of irregularity it is certain that the pulsus alternans and the pulsus irregularis perpetuus are never symptoms of nervous cardiac diseases; they occur only in cases of severe damage of the heart muscle itself. The pulsus irregularis perpetuus is, according to the investigations of Hering, Mackenzie and Gerhardt, nearly always accompanied by the symptoms of severe injury, often of total paralysis of the right auricle. Since we know the important rôle played by the right auricle in the origin and co-ordination of the heart movements, it is not at all astonishing to find complete arrhythmia as a common consequence of its injury. Rather difficult to explain are the short attacks of complete arrhythmia, even of delirium cordis, which are sometimes found in connection with severe indigestion after overloading the stomach with indigestible food. These attacks can often be checked at once by vomiting or by emptying the stomach with the tube. Perhaps they are to be explained as a form of reflex action through the vagus, or they are perhaps of toxic origin.

By far the commonest form of irregularity is that due to the occurrence of extrasystoles. Does extrasystolic irregularity occur in simple nervous cardiac disease? It is said that it does, and Lommel goes so far as to say that extrasystolic irregularity is so common in young nervous individuals that it is of but little importance. I do not agree with this view and I doubt very much whether extrasystolic irregularities are ever to be considered as a sign of purely nervous disorders. Hering was never able to produce extrasystolic contractions in animals when he experimented on the cardiac nerves, but he admits the possibility that extrasystoles may take place by vasomotor influences if these lead to sudden and considerable rise of blood pressure. In this way we can explain the observation that not infrequently slight extrasystolic irregularities exist in young nervous persons in whom no signs of cardiac disease can be detected. But there is no doubt that in the majority of cases the extrasystolic irregularities are due to incipient or advanced disease of the myocardium, to irritable weakness and to a disproportion between the

strength of the heart and the resistance to be overcome. If extrasystolic irregularity is very pronounced, and if a great number of extrasystoles disturb the normal pulse rate, we are always sure of a severe damage of the heart muscle. If this rule is established, are we then allowed to conclude that a rare occurrence of extrasystolic contractions is but a nervous symptom? Such a conclusion would not be logical.

Yet frequently we observe extrasystolic irregularities occurring over many years before any definite manifestations of a damage of the heart muscle or the blood vessels appear. The extrasystoles may even disappear again completely, especially when such injurious influences as abuse of nicotin, strong coffee, overexertion, or the influence of high altitudes cease, or when the heart accommodates itself by means of hypertrophy to the increase of the blood pressure due to the development of arteriosclerosis. If we are able to follow the fate of individuals who have shown in former years extrasystolic irregularity, we may convince ourselves that not a few of them show in later years distinct symptoms of heart failure or arteriosclerosis, and we draw the conclusion that the evolution of those important diseases often extends over more than ten or even twenty years. Therefore it will be better in practice to consider the extrasystolic irregularity as a sign of importance and not simply as a manifestation of a nervous heart, which commonly passes as harmless.

The nervous heart manifests itself very often by troublesome *palpitation*. Here we would emphasize that palpitation must be sharply distinguished from high pulse rate and that not all sensations which are called palpitations by hypochondriacal patients deserve this name. Whenever we are in doubt whether the patient suffers from true palpitations, have him count his heart beat without putting his hand to his chest, the physician meanwhile controlling his count by feeling his pulse. If the patient is not able to feel every heart beat in his chest and to give its exact rate, then he has no true palpitation but some other sensation which he has wrongly interpreted as such.

In true palpitations the heart throbs violently and shakes the thoracic wall so that the observer may feel it with his hand placed over the cardiac region, nay, see it before the patient has exposed his chest. Shall we assume that in palpitation a greater energy is contributed by the heart to the general circulation, or that a larger part of the expended energy is uselessly wasted in shaking the thoracic wall, energy which in the healthy heart is more economically applied to the propulsion of the blood alone? Tracings of the apex beat are apt to give no explanation of the mechanism of palpitation. They show that the ascending line of the cardiogram is steeper and higher, so we may conclude that the systolic

contraction is quicker, that it reaches its maximum more suddenly, within a shorter time and not in that slow way which is the optimum for the propulsion of the blood. According to our own cardiographic tracings, palpitation seems to be produced by a peculiar type of muscular contraction, and this may be due to certain nervous influences.

The cardiographic tracings in nervous palpitation show a close likeness to those of extrasystolic contractions, which also produce the feeling of a shock to the chest walls. In connection with this peculiar form of muscular contraction we observe the fact that the first sound of the heart is louder and accentuated, and this symptom is not difficult to understand when we remember that Ludwig explained the first sound as being produced by muscular contraction and that the first sound becomes less loud and even disappears whenever the systolic contraction is performed slowly. This is the case in aortic stenosis where the cardiac tracing shows a very slow ascending line.

The apex tracings in nervous cardiac troubles show, besides the quick and high ascending line, no uniformity. Sometimes we see a very pronounced flat or even an ascending plateau; in other cases the tracing falls immediately after the first rise and it is not easy to mark the end of the systole. As Hürthle and Frank have shown, we find the ascending type of cardiac tracings whenever the heart has to struggle against a high blood pressure and when the ventricle finds difficulty in emptying itself. The descending type shows, on the contrary, that the outflow of the blood takes place easily and that the resistance in the vessels is not high. We come to a similar conclusion from a careful examination of the arterial sphygmogram (D. Gerhardt). In cases of nervous heart the sphygmomanometric tracings of the radial artery show a high systolic plateau of unusual duration, sometimes even an anachrotic wave. This may be taken as proof that the outflow of the blood through the capillaries is difficult and slow, and this behavior is coincident with a high maximum of arterial blood pressure and a high minimum as well. There is no explanation possible for this observation other than a constriction of the arterioles and the capillaries by means of vasomotor influence. The same behavior is met with in diffuse angiosclerosis. In other cases of nervous palpitation the sphygmomanometric tracings of the radial show a quick descending line, a high maximum, but a low minimum blood pressure; in these cases the outflow of the blood through the capillaries must be considered as rapid and easy.

This leads us to consider the *arterial blood pressure* in nervous cardiac diseases. In healthy non-nervous individuals the blood pressure varies under changing conditions within strikingly small limits. Even

energetic muscular exercise increases the blood pressure but transiently and then not to a very high degree. The difference between the maximum and the minimum (the pulse pressure) becomes greater, but this is merely a sign that during muscular work a greater quantity of blood is thrown out by every ventricular contraction. In nervous and neurasthenic individuals the blood pressure shows the same great tendency to abnormal variations that we have seen in pulse frequency. Muscular exercise, as well as eating and drinking, especially alcoholic drinks, coffee, tobacco, and, above all, psychic excitement, influence the blood pressure quickly and to a greater degree than in normal individuals. So we often observe in our consultations that the mere sight of the blood pressure apparatus is sufficient to produce a certain fear in nervous patients, and that the first readings give an abnormally high maximum of 160 mm. or more. The blood pressure sinks to a normal figure of 140 or 120 as soon as the patient has convinced himself that no injury will be done to him.

This changeability of the blood pressure is often combined with a tendency to flushings of the head and a disagreeable feeling of heat in the face, to attacks of fainting, to headache, and especially to migraine, to sudden perspiration, to cold hands and feet, symptoms which correspond to the disordered condition of the vasomotor system. In such cases the arteries, especially the radial and temporal, show on palpation a marked contraction at certain times, while some hours later they are found dilated, soft and strongly pulsating.

But in some nervous individuals the blood pressure stands permanently at too high a level. We shall seldom be wrong if we assume that this is a sign of beginning arteriosclerosis. Arteriosclerosis is considered to be the result of continued damage to the vessels, due to too great demands on them. Rapid variations in blood pressure and a tendency to abnormally high pressure are among the main causes for the wearing out of the arterial walls. Thus we may understand why so many individuals, who in their youth have shown the symptoms only of nervous cardiac and vasomotor disease, so often fall a prey to arteriosclerosis relatively early in life. How often this is the fate of charming, warm-hearted individuals, with high spirits, quick intelligence and always ready energy, whose end is nephritis, apoplexy or sudden death from angina pectoris! This evolution from primary pure nervous over-excitability of the heart and vasomotor system into severe angiosclerosis is often observed after severe injury to the nervous system by railway accidents, by great grief and distress, often in widows who have lost their husbands under afflicting circumstances. And whenever we see in such cases of nervous

breakdown that the blood pressure continues to be far too high we are aware that arteriosclerosis has set in.

These few remarks may show the importance of the determination of blood pressure. I believe that in the last ten years no other method has brought us such a distinct progress and enrichment of diagnosis as that of the estimation of blood pressure.

The *size of the heart* fails to show any changes in the majority of cases of nervous heart. Indeed the normal size of the heart has often proved a valuable sign in the diagnosis of the nervous type of heart trouble. But we should not forget that among organic diseases also, especially in arteriosclerosis and nephritis, the heart may show for a long period of years normal size to percussion and to Roentgen rays, although it is quite apparent from the high level of blood pressure that it is continually performing increased work and really must be hypertrophied. Simple hypertrophy without dilatation does not increase the dimensions of the heart or only very slightly. On the other hand, it can not be denied that in cases of long standing and severe nervous overexcitement of the heart the myocardium becomes impaired and that true hypertrophy, sometimes also distinct dilatation, occurs. But here we must refer to a source of error. The violent apex beat of the excited heart strikes the chest wall in a much larger area and therefore frequently simulates an enlargement of the heart which really does not exist.

Among the subjective symptoms of the nervous heart we have to remember *pain* and other distressing sensations in the *heart region*. As long as they do not show the characteristics of true angina pectoris these feelings are of very little importance. True angina pectoris is characterized by short attacks of most intense pain. They appear when the patient walks or when he climbs a staircase and force him to stand still until the pain disappears. Very often the attacks come soon after a rich meal, especially if the patient walks soon afterward; sometimes the attacks occur during the night and awaken the patient from sleep. The pains are localized in the precordial region, behind the sternum, or in the epigastrium, and sometimes may be mistaken for gastric pains; they almost always radiate to the left or the right arm or to the carotid region of the neck. In simple nervous cardiac disease the painful sensations are of far longer duration. They are not dependent on walking, eating, etc., and do not appear during sleep. In most cases they are not at all severe. Usually they are localized in the region of the apex beat, and very rarely radiate to the arms. Very often the patient has the impression that the painful sensations of the nervous heart have their seat not in the heart itself but in the tissues covering the thorax,

and frequently we find a distinctly hyperesthetic area over the skin in the region of the apex beat. If the pressure of the stethoscope alone suffices to call forth expressions of pain from a female patient, then the physician may be sure that he has to deal with a hyperesthetic patient and not with a symptom of true cardiac disease. Though the painful, or better the disagreeable, sensations in the heart region are commonly of but little intensity, they are not to be neglected. By their continued presence they irritate the patient and remind him of his heart the whole day long. As a rule we can say: the more the sensory symptoms, pain or palpitation prevail, the more the psychic factor is pronounced, and the more the patient is subject to the hyponchondriacal idea that he is suffering from severe heart failure.

It is a question whether the well-known symptoms of true angina pectoris or of pseudoangina are met with in simple nervous disease, and whether we should agree with Huchard, Rosenbach and Romberg, who regard attacks of the anginal type as especially characteristic of nervous cardiac affections. Are we able to distinguish a pseudoangina pectoris from the true one, observed in coronary sclerosis and aortic disease? Certainly some nervous patients describe attacks of cardiac pain or even of agony, which makes us believe them to be of great importance. But if the physician happens to observe such an attack personally he can usually convince himself that the attack does not present that elementary convincing severity which characterizes the pains of true coronary sclerosis, but that it is more a feeling of nervous anxiety and oppression. Indeed I am inclined to doubt that there exists a true angina pectoris as a symptom of mere nervous affections. I believe that every patient who has suffered from typical angina pectoris is to be suspected of having some dangerous organic disease and of being prone to sudden death.

It is never wise to make the diagnosis of a purely nervous cardiac disease when symptoms of actual circulatory incompetence are present, i. e., dyspnea, cyanosis, swelling of the liver, diminished quantity of urine, etc. Usually the nervous cardiac and vasomotor disturbances are characterized by polyuria with clear light-colored urine, and very often by the interesting phenomenon of phosphaturia, i. e., by diminished acidity of the urine.

As far as the dyspnea of nervous patients, especially of young people, is concerned, their craving for air and their supposed inability to draw a full breath, the experienced eye of the practitioner should have no great difficulty in distinguishing its true hysterical or hypochondriacal nature.

We now turn to an especially important subject, namely, to the consideration of some other cardiac diseases which show symptoms similar to those of the nervous affections and which are often mistaken for them. I am inclined to say that the majority of cases which in former years have been considered as typically nervous can no longer be placed under this heading.

Here we have first to mention the heart affections in *goiter*. This is very common in the southern parts of Germany and in Switzerland, and from my own experience I may say that nearly a third of all cases of so-called nervous palpitation belong to this disease, viz., to hyperthyroidism. Here I do not mean the fully developed cases of exophthalmic goiter, but those far more frequent cases of incomplete hyperthyroidism where only the cardiac symptoms are very prominent and where other symptoms seldom or never attract the attention of either the patient or physician.

The "*Kropfherz*" (Fr. Kraus) or hyperthyroid heart can be distinguished from the nervous cardiac affections by the fact that the high pulse rate lasts throughout the whole day and night and is not due to reflex action alone. The acceleration in most cases of goiter heart is not excessively great, 90 to 120, not nearly as high as in paroxysmal tachycardia, but high enough to trouble the patient constantly and to make him unfit for all continued work. This effect is due especially to the fact that palpitation is very pronounced. It is worth mentioning that in the hyperthyroid heart as well as in fully developed exophthalmic goiter the increased pulsation is especially felt over the region of the right ventricle, that is, along the left border of the sternum as high as the second interspace, and at the autopsy in cases of exophthalmic goiter I have observed that there was present a marked hypertrophy and dilatation, especially of the right ventricle, and an excessive congestion of the pulmonary vessels. The blood pressure does not depart from the normal. Vasomotor symptoms, flushings of the head and sudden perspiration are very common. If we carefully examine the patient we rarely miss a fine tremor of the fingers and a certain psychic over-excitability. The patients are in a permanent state of distressing mental irritation. They complain that they get tired and worn out by any mental or muscular exertion, and that they are unfit for continued effort. Often we see young individuals who experience difficulty in school or in their occupations in whom hyperthyroidism explains the psychic and bodily deficiencies. Sometimes in the case of young women and girls one is led to suspect chlorosis, but the blood shows normal composition, and the lassitude and cardiac palpitation, in combination with a soft swelling of the

thyroid gland, lead the physician to the right diagnosis. Very characteristic is the liability to lose flesh, even while the appetite is good. In the course of months and years under alternating improvement and aggravation we sometimes see the development of dilatation and incompetence of both ventricles and every symptom of cardiac failure, edema, oliguria and severe dyspnea. The same poison which for many years caused only an increase in the number and strength of the cardiac contractions proves finally deleterious to the myocardium.

The diagnosis of hyperthyroid heart is easy when the thyroid gland shows the characteristic soft swelling, even though this be but slight. The diagnosis is difficult when no swelling at all is present. Yet we sometimes see cases which show every characteristic of hyperthyroidism, though no enlargement of the gland is present. As we may suspect kidney disease when no definite signs are present, so may we believe that a morbid state of the thyroid can exist without any apparent enlargement or diminution in the size of the organ.

In cases presenting diagnostic difficulties we can usually come to a conclusion by a careful administration of the iodids. In cases of hyperthyroidism the iodids, even in the smallest doses, cause immediately a marked change for the worse. They produce an increase of palpitation, a diminution in weight and the appearance of nervous excitement and tremor. I can not agree with those authors who distinguish special types of the goiter heart supposedly due to mechanical pressure by the enlarged gland on the vagus and sympathetic nerve. Rather I am convinced that the goiter heart is an entity and is due to an excessive formation and absorption of the secretion in the thyroid gland. Experiments on the isolated mammalian heart have shown that thyroid extract causes an increase in the number and strength of contractions, and the proof that palpitation, tachycardia, vasomotor symptoms, mental excitement, and the characteristic increase of metabolism are really due to hyperthyroidism, has been given by the fact that the medicinal administration of preparations of the thyroid gland produces in normal individuals the same symptoms, and that in some (but unfortunately not in all) cases of hyperthyroid heart the symptoms are relieved or removed altogether by extirpation of one lobe of the gland. So we may place the "Kropfherz" or hyperthyroid heart among the toxic processes.

Among the poisons which act on the heart there is to be mentioned *caffein*. In connection with this we must consider the excessive use of coffee and tea. Caffein is sometimes used in Germany for the purpose of simulating nervous irritable heart and thus offering escape from military service. Caffein, indeed, when used in large doses, produces exactly

the same symptoms as nervous cardiac overexcitability, strong palpitations and pronounced psychic disturbance.

Tobacco must also be mentioned. I purposely do not say nicotin, for recent investigations make it very questionable whether the toxic effects of tobacco run parallel to its content of nicotin. Nicotin is a strong poison to the nerves, and Langley has shown that it paralyzes the sympathetic ganglion cells. Nicotin acts on the isolated mammalian heart, increasing the rate and intensity of contractions. Tobacco affects the normal heart much less than the nervous or weakened heart. In nervous individuals it produces a distinct increase of the blood pressure. Though chronic abuse of tobacco is surely deleterious to the heart, it proves yet more dangerous to the blood vessels, and in no small number of cases of early and general arteriosclerosis, especially of the coronaries, the abuse of tobacco is the primary cause. Sometimes tobacco seems to produce attacks of pseudoangina pectoris or, as Gibson correctly says, the symptoms of stenocardia without coronary sclerosis. It is possible that a temporary spasm of the coronaries may be produced by the influence of tobacco.

Concerning *alcohol,* we know that it affects the vessels less than the heart muscle, and that the different kinds of alcoholic drinks affect the heart muscle very differently. Decidedly the worst of the alcoholic drinks, as far as the heart is concerned, is beer. The poisonous effects of alcoholic drinks are especially seen in women and children. How often does a woman, a child, a pupil pass for a long time as nervous and affected with nervous palpitation until the experienced physician discovers the alcoholism! It must be noted that in women, in young people and in all individuals with weakened hearts and feeble nervous systems very small quantities of alcohol act deleteriously and produce palpitation. Nervous individuals often show very pronounced intolerance for alcohol. A glass of wine is enough to produce disagreeable flushes and hyperemia of the head, throbbing of the pulse and insufficiency of circulation after any considerable muscular exertion, so that the patients themselves soon realize that they must avoid all alcoholic drinks. But it would be erroneous to suppose that alcohol produces cardiac and vasomotor disturbances and nervous excitement only in women, in young or feeble individuals and in convalescents; it causes the same symptoms also in cases of chronic alcoholism in men. The chronic drunkard very often shows the symptoms of irritable weakness of the heart in combination with general nervous over-excitability, and it is often difficult to find out the true nature and origin of such a "nervous heart" if the patient does not confess his former alcoholism.

When we are considering the toxic agencies acting upon the heart we must not forget the *bacterial toxins*. After infectious diseases, severe scarlet fever, typhoid fever, and especially influenza, there remains often, not only for months but for a year and more, a state of cardiac impairment which closely resembles the irritable heart of nervous individuals. Any excitement or exertion produces an increased pulse rate and distressing palpitation. But muscular work leads in such cases not only to palpitations but also to dyspnea and a feeling of oppression which makes it impossible to continue the work.

The history alone in such cases may lead to the realization that we have to deal not with a nervous heart but with one weakened by infectious disease, although sometimes the patient himself has nearly forgotten that his heart failure dates from the recovery from acute disease. In other words, the injured and enfeebled heart responds to all impulses with abnormal irritability and the "irritable heart" is, so to speak, often nothing else than a weakened heart.

In this connection we must mention also the excessive cardiac irritability and acceleration seen in many patients with *tuberculosis*. The toxic products of the tubercle bacillus act on the heart as well as on the temperature. In cases of debility and of loss of weight, combined with palpitation and slight elevation of temperature, the physician will often find the greatest difficulty in judging whether the case belongs to hyperthyroid or nervous heart or to beginning tuberculosis, especially since tuberculosis in its earliest stages is so extremely difficult to diagnose. Yet it is well to remember that in tuberculosis the heart appears commonly very small in size when examined by Roentgen rays, and that the blood pressure is below the normal level. Tuberculin injections may help the diagnosis. As a result of a prolonged rest cure in tuberculosis we sometimes see that the heart becomes more and more feeble and irritable. Too long continued confinement to the bed or the reclining chair weakens the heart decidedly and makes it unaccustomed to adapt itself to muscular exertion.

The disturbances of the heart which we see frequently in connection with *affections of the sexual organs* deserve especial attention. In pregnancy, especially during the first three months, we not infrequently meet with arrhythmia of the extrasystolic type, which is sometimes believed to be of nervous origin; but, as we have mentioned above, extrasystolic irregularities should rather direct our attention to the myocardium than to the nervous system. We see heart affections manifesting themselves in connection with pathologic processes of the uterus and its appendages, especially in myoma and in inflammatory exudations and adhesions, to

a much higher degree than in the normal state of pregnancy. Cardiac disturbances, tachycardia and arrhythmia appear or increase during the menstruation, and they sometimes pass during this period to actual delirium cordis. If we find in a case of myoma a heart which is not able to withstand chloroform narcosis, which suddenly stops during or soon after operation, and which finally appears at the autopsy as a flabby, soft organ, we may be sure that this is the final stage of a condition which in its beginning had for years wrongly been called nervous cardiac trouble.

In further connection with the sexual organs stand undoubtedly the so-called nervous palpitation, the cardiac and vasomotor disturbances which occur in the climacteric period. Besides palpitation and occasional cardiac enlargement there appear often most disagreeable vasomotor symptoms, which lead to all kinds of falsely interpreted organic sensations and excitements, and the same symptoms may appear, even to a much greater extent, when after the surgical removal of the sexual organs a premature climacterium is produced in younger women. I have often observed in the cases of climacteric cardiac affections that the blood pressure was raised to a high degree.

At the beginning of sexual development, in boys as well as in girls, there often occurs pronounced excitability of the cardiac action, with strong palpitation, and sometimes with enlargement of the area of heart dulness and loud murmurs. These murmurs lead to diagnostic difficulties and to the erroneous supposition of a valvular disease. This *heart of adolescence* may lead to stormy manifestations, especially when the sexual desire undergoes an unnatural excitement and gratification. The heart of masturbation, which Krehl has described, is not a rare thing.

It is rather difficult to explain the connection between the sexual organs and the cardiac and vasomotor system. Is it a reflex mechanism going through the nervous paths or is there an inner secretion from the sexual organs like that of the thyroid or the suprarenal gland? The experiments of the last years, especially those of Starling, give more emphasis to the second hypothesis. Yet we see in all these cases that nervous symptoms are very prominent, sometimes of a hysterical character, and there is no doubt that the sexual heart affections occur especially in individuals with nervous constitutions.

Not infrequently do we see in connection with *obesity* a certain irritability of the heart, often years before the symptoms of true cardiac failure appear. A quick pulse rate is met with particularly in those obese individuals who are unaccustomed to any physical exercise, who drive instead of walk and avoid all muscular exertion. Muscular strain

produces in such patients a high pulse rate, palpitation, and sometimes some cardiac oppression. The patients themselves are very often inclined to think that they are suffering from nervous heart, especially those who do not like to admit that they are too corpulent. But this is not a nervous heart; it is in truth the weakened or *untrained heart* of the unexercised individual. The strength of the heart stands in some relation to the strength and development of the other muscles of the body. A loss of general muscular strength, whether it be due to disease or starvation or to want of exercise, is commonly accompanied by a loss of cardiac strength, and there is no better way to increase the strength of the heart than by carefully regulated general muscular exercise.

We have seen how many pathologic conditions may simulate the nervous heart and how easily an error of diagnosis may arise. Indeed, it must be acknowledged that the more thoroughly a physician examines his patients the more rarely he will come to the diagnosis, "nervous cardiac affection." This diagnosis is only permissible after the exclusion of every other possibility. It would surely be erroneous to deny altogether the existence of the nervous heart, but we must insist that this diagnosis be made only when proof is afforded that there is no failure of the cardiac muscle present, and where the history and examination of the patient shows the presence of general nervous irritability and debility, for only in markedly nervous individuals can we base cardiac disturbances on the nervous system alone, and only then when the cardiac symptoms show the clinical character above sketched.

Paroxysmal tachycardia is rightly included among the nervous diseases of the heart. Suddenly, and often without previous warning, a cardiac frequency of 160 to 200 or more beats sets in, and after some hours or some days the normal rhythm is suddenly restored, often accompanied by the eructation of gas. Paroxysmal tachycardia may represent a primary nervous disease and is then closely connected with migraine and sometimes with its worse brother—epilepsy. I believe that paroxysmal tachycardia is often to be considered as an anomalous or disguised form of these strange diseases, and it shares with them the uncertainty and the hopelessness of therapy. Some fatal cases have been reported where paroxysmal tachycardia was connected with syphilitic changes or other organic derangements in the vessels of the basis cerebri and the medulla oblongata. Sometimes attacks of similar character appear as a complication of already existing organic valvular or myocardial disease. If by chance we can observe the onset of such a tachycardial attack we can readily recognize that first single, and soon more and more frequent interpolated systolic contractions appear during diastole, till finally the

heart rate is exactly doubled or quadrupled. Not only the diastolic rest but also the systolic contractions become very short, and we remember from experiments that the shorter the contractions the shorter becomes the refractory period of inexcitability.

The manifestations of paroxysmal tachycardia can not be otherwise explained than by the hypothesis that through central nervous influence the irritability of the heart muscle increases to a very high degree, although it is not yet possible to explain by what particular mechanism those influences appear so suddenly and disappear at once again.

Every lecture on a clinical subject should conclude with a consideration of *therapeutics,* since all our efforts, scientific research as well as practical work, are directed toward the single aim—to help sick mankind. In the case of true nervous cardiac affections it may be said that treatment which is directed toward the heart itself almost never results in benefit. Indeed, digitalis, caffein, strophanthus and other similar remedies rather do harm than good and they are not able to diminish the increased heart rate and palpitation. Yet there is an exception to this rule; if a primary nervous cardiac disease has finally led to actual cardiac insufficiency, to dilatation, edema and arteriosclerosis, then the above named remedies, and especially also the diuretics, prove of great value.

The treatment of the true nervous cardiac diseases must be directed exclusively against the general nervous condition, and particularly we must try to remove its cause, whether it be overwork or indulgence in excitement of any kind. Above all, we have to remove the patient from the environment, the "milieu," which has provoked nervousness, and that is very often his own family. A sojourn in an agreeable and quiet country place may be of the greatest benefit. High altitudes, such as Switzerland or the Tyrolese mountains, especially are apt to bring great improvement, while the seashore, on the contrary, often proves to have no good influence. The study of climatic influences deserves much attention. Altitude in particular has a most wonderful effect on the heart, the blood vessels and the blood itself, and individuals with nervous constitutions and with cardiac and vascular diseases are very markedly affected by it.

It is not wise to send nervous patients to watering places like Nauheim and to treat them with such measures as carbonic acid baths or alternating electric currents. Such "cures" should be avoided because they prove more exciting than calming, and because they direct the patient's attention too much to his heart, and bring him to the fixed idea that his fears of an organic cardiac disease are correct, and that the doc-

tor speaks of a nervous affection only to console and to deceive him. Very often we see that a nervous and hypochondriacal patient distrusts the physician who simply and truly declares that the heart is normal and the whole trouble a nervous or imaginary one, and much prefers to believe the one who says the heart is seriously attacked, who strengthens the patient's fears and undertakes long and strenuous cures not at all to the patient's benefit.

Sometimes in such cases of hypochondriacal ideas it proves useful to outline the size of the heart by orthography with Roentgen rays, and to convince the patient from this diagram with the centimeter scale that the pretended dilatation is absent. But when we succeed in winning the confidence of our patient we must try to turn his attention away from his heart, to raise other interests and thoughts. For this purpose carefully directed muscular work, gymnastic exercises, walks, and even a little mountain climbing and every kind of outdoor treatment, are most useful. For in the true nervous cardiac affections muscular exercise has not a harmful but a good influence on the heart. Per contra, rest cures which are of benefit in every organic cardiac failure do harm to the nervous heart, really weakening it and making it more and more unfit to adapt itself to any strain. Eventually we may be able so to educate our nervous patient that he learns to keep his feelings and emotions under proper control. This stage once reached he may also be able to command to a certain extent the involuntary emotional movements, excitements and reflex actions of his inner organs so that he may no longer be a victim of their effects.

THE HEMOLYTIC REACTIONS OF THE BLOOD IN DOGS AFFECTED WITH TRANSPLANTABLE LYMPHOSARCOMA.*

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During the course of the present year I reported a series of experiments[1] on the hemolytic properties of extracts from organs and from tumors of dogs. I showed at that time that two sorts of hemolytic substances could be extracted from tumors. One of these, which was present in undegenerated tumors, was thermolabile, and hemolytic only when activated by a substance extracted from the red blood cells. This first substance is comparable to a similar hemolytic amboceptor present in certain normal organs, e. g., kidney. At about the same time and independently it was shown by Friedmann[2] that a hemolytic substance could be extracted from the pancreas, which destroys the red blood cells of the same species, when complemented by some substance (probably of the lecithin group) present in the serum of certain other species. The second type of hemolysin is present only in necrotic tumors; it acts as a simple hemolysin, needing no complement. I ventured to suggest in my first paper that it is the second group of substances which probably passes into the blood, thus contributing to the anemia and the cachexia of malignant tumors.

Since that time I have had the opportunity, thanks to the kindness of Dr. S. P. Beebe, of prosecuting this investigation along somewhat different lines. I have had at my disposal dogs inoculated with the same strain of tumor previously studied, in every stage of its growth. In some the tumors were actively growing, in others they were regressing, while still others were overcoming their tumors as the result of a passive immunity conferred by transfusion. Some of the dogs were in good condition; others were cachectic to the last degree. At the same time I have had a large number of dogs not affected with these tumors, for comparison; some of the latter have been healthy, some cachectic.

It was the object of the present research to study the serum of dogs which had been inoculated with tumors, and to determine whether it possessed any of the hemolytic power characteristic of extracts made

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1. Jour. Med. Research, Boston, 1907, xvi, 287.

2. Deutsche med. Wochschr., Leipsig u. Wien, 1907, xxxiii, 585.

from the tumors themselves. In withdrawing blood from these animals and separating it into serum and corpuscles for further study, the following observation was made: It was generally found that the serum obtained from animals with tumors was stained with hemoglobin, whereas that obtained from animals not having tumors was of the normal straw color. In other words, during the process of separating out in the icebox, the serum of tumor animals had destroyed a sufficient number of its own corpuscles to give it the characteristic tinge of hemoglobin. At the same time, emulsions of corpuscles from the same animals in salt solution remained unchanged, demonstrating that the hemolysis was due not to the lowered vitality of the corpuscles, but to the hemolytic quality in the serum.

The next step was to determine the effects of definite amounts of serum both of normal and of tumor dogs on their own and on other corpuscles. For this purpose, twenty-five dogs in all were selected, of which eleven had tumors and fourteen had no tumor history. All of these dogs were treated in the same fashion. The femoral artery was laid bare under morphin anesthesia, and from twenty to thirty cubic centimeters of blood was obtained from it. The major portion of the blood was allowed to coagulate for the purpose of obtaining serum, while the rest of it was shaken up with glass beads, centrifuged, and made up into a 1 or 2 per cent. suspension in normal salt. The sera, and the corpuscles thus obtained on one day from a large number of dogs, were tested on one another on the following day. One cubic centimeter of serum was always added to an equal quantity of red cell emulsion, incubated for a few hours and transferred to the icebox, where it was allowed to remain over night; the results were noted the following morning. In this manner, 226 separate serum-corpuscle combinations were examined.

A record of one of the experiments will indicate better than any amount of description the type of result which was regularly obtained. The description of the dogs made use of in the experiment, and indicated by numbers in the table, is as follows:

Dog 455.—Four tumors growing slowly for six weeks. Condition good.

Dog 509.—Four tumors growing for two weeks very rapidly. Thin.

Dog 460. Spontaneous recovery from tumors, which were three in number, and were very rapidly absorbed six weeks before the experiment. Very cachectic animal.

Dog 244.—Tumor almost completely absorbed, owing to repeated transfusions. Dog very cachectic.

Dog 458.—Spontaneous recovery from tumors. In fine condition.

Dogs 516, 517 and 518.—Normal.

Dog 520.—Cachectic. No tumor history.

The following table shows the comparative hemolytic effects of serum from normal and tumor dogs on corpuscles. One c.c. of serum from each animal was mixed with 1 c.c. of corpuscles of each animal, in emulsion. The record of each serum reads along the horizontal line.

	CORPUSCLES.						
	1-455	**2-509**	**3-458**	4-517	5-518	6-516	7-520
Serum **I 455**	—		—	v. sl.	v. sl.	v. sl.	v. sl.
Serum **II 509**	—	—	—	sl.	sl.	sl.	sl.
Serum **III-460**	+	+	+	+ -	— +	++	- -
Serum **IV-244**	+	— —	-	+++	+++	— + —	— — -
Serum **V 458**		—			sl.	v. sl.	sl.
Serum VI-518	—	—	-	—			
Serum VII-520	-	-	-	—	—		—

NOTE: — denotes negative reaction; v. sl. denotes very slight reaction; sl. denotes slight reaction; + denotes moderate reaction; ++ denotes strong reaction; +++ denotes complete reaction.

If the table be interpreted in the light of the preceding data, the following conclusions may be drawn from it:

1. The serum of all the tumor dogs is distinctly more hemolytic than is the serum of non-tumor dogs. Of the tumor animals, the two cachectic examples (460 and 244) are more actively hemolytic than are the other three.

2. There is a distinct difference in the resistance of the various corpuscles to the destructive activity of the sera. The corpuscles of the tumor animals are always more refractory than are the normal; they break down less rapidly and less completely.

These two phenomena, the hemolytic activity of the sera and the resistance of the corpuscles of tumor animals as compared with other dogs, dominate the entire series of experiments.

The cause of this difference has seemed to me to be a matter of some importance. It might conceivably be due to a difference in the tonicity or content in electrolytes of the serum, resulting in some obscure manner from the growth of the tumor. In order to determine this matter, each set of corpuscles was in every experiment subjected to the action, not only of a normal salt solution, but also to one of a 0.4 per cent. and one of a 1.6 per cent. strength. It would seem that the degree of anisotonicity represented by these solutions must far exceed that of any serum obtained from a living animal. Nevertheless, the activity of the resulting hemolysis was in no way comparable to that produced by the sera. The general condition of the animals can not be held

responsible, inasmuch as some of the controls were much more emaciated and cachectic than some of the tumor dogs. The hemolytic power of the serum resides, therefore, in some other factor, at present undetermined—possibly the same toxins as were extracted from the tumors in the experiments which I previously reported.

The apparent coincidence of poor general condition and marked hemolytic activity is quite striking, and might at first sight impose as a "*propter hoc.*" It has, however, been pointed out that dogs in worse general condition, but without tumors, show less activity in hemolysis. On the other hand, it is perfectly justifiable to interpret the "poor condition" as a resultant of the toxic character of the circulating serum, which manifests itself in the test tube by hemolysing the contained red cells. Two exceptions occurred to the general rules above described. Dog 125, whose tumors had regressed owing to three successive transfusions, in good condition, possessed a serum of slight hemolytic power and corpuscles of slight resistance. Whether this was due to the predominance of normal blood in his vessels, I leave undecided. The second case, Dog 638, normal, has a markedly hemolytic serum, but non-resistant corpuscles. This dog had proved naturally immune to a sarcoma implantation. It may also seem contradictory that dogs which had recovered from their tumors, either spontaneously or as the result of transfusion, should still retain the hemolytic character of their serum to an excessive degree. The fact is, however, in accord with what is known of the clinical absorption of tumors. If, owing to an excessive use of *x*-rays or the mixed toxins, a tumor breaks down too rapidly, its absorption may lead to extreme intoxication of the organism, and even to death. Thus the disappearance of the tumor goes hand in hand with the circulation of the toxic products which have been absorbed. How long an animal may retain these products in his circulation is still to be determined.

The bearing of these experiments on the problem of the anemia accompanying malignant new growths is manifest. They demonstrate that the growth of tumors causes the development of toxic qualities in the blood serum, the exact nature of which has not been determined. It is suspected, however, to be due to the absorption of hemolytic substances previously demonstrated in the tumors themselves.

The bearing of these experiments on the practice of transfusion in curing the tumors of animals, or of men, is important. As is well known, the operation has been performed a number of times in dogs with some success. It is quite evident, however, that to mix the blood of dogs, either of which is hemolytic for the other, would entail the destruction

of a very considerable number of corpuscles, and so would, in part, defeat the very object of the transfusion. There can be no question that the test-tube reactions may be taken as a very good indicator of what would happen were the same bloods to be mixed *in vivo* by transfusion. Of this fact we have had indubitable evidence in the hemolysis resulting after transfusing the blood of one dog into the vessels of another whose serum had been shown to destroy the corpuscles of the former in test-tube experiments. (These experiments have not yet been published.) It is clear, therefore, that every transfusion should be logically preceded by test-tube reactions, and that only those animals should eventually be selected whose serum and corpuscles are mutually tolerant.

On the bearing of the experiments on the subject of human disease I must, for the present, forbear to enter. A considerable number of observations already completed go far to indicate that the results in dogs illustrate conditions which have a parallel in the blood of human cancer cases. On this important point, however, much information must be collected before final conclusions can be drawn.

My thanks are due to Dr. Beebe for his constant encouragement and help during the course of this research.

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TRICHOMONAS HOMINIS INTESTINALIS; A STUDY OF ITS BIOLOGY AND ITS PATHOGENICITY.*

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Of the parasitic protozoa that infest the gastrointestinal tract, the flagellates merit more attention than is usually accorded them. American observers, who have interested themselves in gastro-intestinal parisitology, and particularly with the monocellular group of organisms, have attached little importance to this by no means uncommon group. English writers, too, have published scarcely any reports of intestinal diseases with which this class of organisms is associated. Continental clinicians, on the other hand, have been more active. Every now and then reports of cases of "intestinal catarrh," "protozoan diarrhea," and the like, find the flagellates playing a not inconsiderable rôle.

The flagellates come under the large group of *Plasmodroma* (Doeflein), and are of the class of *Mastigophora* (Diesing). We find the subclass of *Flagellata* (Bütschli) divided into two divisions of *Monadina* and the *Isomastigoda*. Of the former the *cercomonas* is the representative. The latter is divided further into two families—the *megastoma entericum* (Grassi), typifying the *Polymastigina,* and the *trichomonas* (Donné), typifying the *Tetramitina.* The species of *Trichomonas* that interests us particularly in this study has further been subdivided by some authors according to their morphology or according to the part of the body in which they are found.

We are indebted to Donné, who discovered the parasites in gonorrheal vaginal secretions, for the first accurate description. Trichomonads have since been found in other parts of the body, and in their early history usually associated with some pathologic process. Owing to imperfect observations and, at times, faulty descriptions, these protozoa have been confounded with the *Cercomonas* of Davaine, with the *Megastoma entericum,* and, in one instance, with the *Balantidium coli.* Much of this confusion was due to the inferior methods of observation employed at that time. Other workers, even in recent years, unacquainted with previous work on the organisms, have given them different names, so that many of the reports are misleading.

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* From the Medical Clinic of Prof. George Dock.

Leuckart, in 1863, did more to untangle the conflicting ideas than any one other investigator. But clinicians, particularly, still persisted in naming these organisms after earlier writers. Ekecrantz and Tham's parasites were undoubtedly cercomonads identical with the smaller forms described by Davaine. Marchand found in them a case of typhoid fever and, though without undulating membranes, they doubtless were trichomonads. Grassi endeavored to make finer distinctions than had previously been attempted, and was forced to name some "new" forms. Thus *Monocercomonas hominis* and *Cimænomonas* sprung into the literature. Most of the parasites in his 100 cases were trichomonads. In Leukart's second edition of *"Die Parasiten des Menschen"* we find an accurate classification which the additions of Cunningham in 1881, and Blochman a few years later, did not materially improve on, but substantiated in all important details.

The most important habitats of the trichomonad have been in the intestinal tract and vagina. In the latter place they have never had any pathologic meaning; in the former their presence has given rise to many conflicting opinions as to their significance. Other organs of the body have been infected by them, and much of the interest that is attached to the parasites has grown out of their presence in such localities. Kannenberg, Litten, Streng and Schmidt have found them in tuberculous and non-tuberculous cavities of the lungs. In recent years Rappin, Leyden and Prowazek have come across them in the oral cavity, while in 1904 Theobald and Galli-Valerio observed these flagellates in cases of carcinoma of the jaw. Kruse and Pasquale, Lambl and Cunningham have found them associated with other parasites in cases of liver abscess. A most uncommon and unique case is reported by Hunt, in which the trichomonads occurred along with streptococci in a walled-off perineal abscess. It is only during the past few years that the finding of flagellates in stomach contents have been reported. Hensen in 1897 encountered the trichomonad in a case of carcinoma of the cardia. Since then Strube, Leyden Cohnheim, Rosenfeld and Zabel have met with the trichomonad under like conditions. Emerson believes that it has a distinct diagnostic value in such cases.

It is the occurrence of this organism in the intestinal tract that interests us most in this paper. Ingested with the food, the trichomonad probably thrives best here, in an alkaline medium. For this reason, and because the feces are here in a liquid state, the small intestine no doubt harbors most of these parasites. It is, therefore, in the freshly passed feces in all cases of enteritis that we should seek them. It was especially after Roos' work that more active search was made for flagellates in

diarrheic stools. Though Cahen in 1891 found a cercomonad in a six-months-old babe, Epstein's series in children was the first in which a pathogenesis was strongly suggested. His excellent report on Monocercomonas Diarrhea was followed by the groups of cases of Kruse and Pasquale, Piccardi, and Schürmayer. Janowski's discussion of the subject of flagellate diarrhea in 1897 is the most comprehensive review that has appeared. Skaller in 1898 contributes a case of much interest, and follows with numerous opinions regarding the action of the trichomonad on the intestinal wall. Ucke was the next observer to interest himself in these organisms. He reported the largest number of cases, forty, in which the trichomonad was associated with diarrheic stools. Osborn found the trichomonad in a case from this clinic along with the ameba and two larger parasites. Terry in 1905 is the only American writer, so far as I can learn, who has made any observations on trichomonad diarrhea. The cases that he reported before the Chicago Pathological Society are of importance. During the year 1906 Castellani, Biland and Krause published their observations on several unusual cases. That of Biland is of value especially in that it contains strong arguments for the pathogenesis of the trichomonad. New text-books appearing during the past few years have given more attention to these intestinal flagellates, so that a perusal of many of these will convince one of the growing clinical importance of the trichomonad.

To unravel the faulty nomenclature that has woven itself about the trichomonad, both from the improper regard of previous work and from faulty observations, would be unprofitable. Such terms as *Monocercomonas hominis* (Grassi, Epstein), *Cimænomonas* (Grassi), *Bodo urinarius* (Hassall), *Cercomonas coli hominis* (May) should be discarded. They are all one and the same, and the term trichomonas is fitting for them all. Recent observers have considered the *Trichomonas intestinalis, vaginalis hominis pulmonalis,* etc., different forms. Prowazek, especially, finds distinctive marks of differentiation. The majority of investigators do not agree in this, however, and from the descriptions of authors who have examined the various forms with care I can discover no essential differences. The most striking that I met with were the variations in the undulating membranes that were long in all of my cases and are usually described as extending along only a part of the body in the *T. vaginalis.* I have been unable to get material for comparative study, but, relying on the recent and trustworthy descriptions of Janowski, Dock, Schaudinn, Cohnheim and Schmidt, I am led to the conclusion that we should place all these forms under the genus *Trichomonas* as classified originally by Braun.

Against the fact that these flagellates are the same as those found in lower animals, much evidence exists. Inoculation experiments from man to lower animals, as will be described later, have notably failed. Moreover, their structure is in many ways dissimilar and their mode of reproduction unlike. Hence I am strengthened in the belief that the designation of the entire group of trichomonads found in man under the group of *Trichomonas hominis* is justifiable. The appending of their abode would then be a matter of choice, serving merely as a more complete classification for comparative work.

Morphology.—Though much has been written on the morphology of these parasites, their finer structure still invites investigation. Nor are all the grosser details of these parasites definitely settled. A glance at the many drawings by as many different observers is proof of the insufficient work that has been thus far carried out. In outline the trichomonad resembles, roughly speaking, an apple seed. It departs, however, from this form in a variety of ways, assuming elliptical, spindle, pyriform, irregularly elongated, comma-like and globular shapes. When actively motile, it is continually varying its outline, as it accommodates itself to its surroundings and its direction of motion. The smaller forms preserve the more typical outline, whereas the larger ones generally manifest the more grotesque. The body is perfectly rounded, not flattened as many have observed. Of this I have no other proof than that, as often as I have seen the body, either from its anterior or posterior pole, it has never presented any other than a globular form.

The size of the trichomonad is as variable as its outline. The young forms are the smaller, whereas the mature trichomonads are at times of unusual size. It is of interest to compare the measurements of several observers:

Marchand	13x7.5 9 microns	tail	3 microns
Miura*	17x12 microns	tail	6 microns
Dock	15-22x10-15 microns		
Blochmann	15 23 microns		
Bouchard	10-15x7-10 microns	maximum length	30 microns
Bütschli	up to 40 microns		
Davaine	8-10 microns		
Donné	8-18 microns		
Galli-Valerio	18-19x9-10 microns		
Krause	13-15x7-8 microns		
Leukart	10-15x7-10 microns		
Prowazek	12-24x8-16 microns		

* He gives the flagella from 8 to 10 microns in length.

Accurate measurement is well-nigh impossible in a normal active trichomonad. A loss of motility on its part means an alteration in its vitality as well as form. Then, too, the length of the tail must be

added to that of the body, as the division between the tail and the body can not be determined with certainty in the active form. I have made a series of measurements whose average tallies with that of Prowazek, Dock and Miura. The smallest form that I encountered was 9 microns in length and 6.5 microns in width. The largest was 32 microns long and 19 microns wide. The average organism was 17 microns in length and 10 microns in width. That the same organism, on account of its labile protoplasm, can increase its length and decrease its width and vice versa is obvious.

The organism is distinguished in its active state by the refractive powers of its protoplasm. It has a distinctive sheen not unlike a bit of ground glass, held up to strong light. With highest amplification the protoplasm shows fine granulations resembling very closely the protoplasm of an unstained leucocyte. When the organisms grow older the granules are darker, either coalescing to form more distinct masses, or appearing more distinct in contrast to the minute vacuoles that form in the protoplasm. I have never been able to see a limiting membrane either in living or in stained specimens. When a weak corrosive sublimate solution is allowed to touch the organism the part first affected suddenly coagulates as any albuminous substance will, and gives the appearance of a cuticle. This is but momentary, for the same action quickly extends to the remainder of the protoplasm. There are, however, two distinct parts to the cell that can be differentiated. The ectoplasm is a transparent homogeneous layer. The flagella, the undulating membrane and the tail spring from and are a part of the ectoplasm. The flagella are very delicate, narrow and continuous with the granular ectoplasm in the healthy organism. Carefully stained specimens, under high amplification, show them to be a part of the above named structures that are concerned in the motive powers of the organism. With any of the eosin-methylene-blue stains they assume a pale, grayish-pink hue. The ectoplasm is capable of motility in any part, as is shown by the formation of pseudopodia in some forms during the late stages in life, and it can resist the destructive influence of reagents longer than the endoplasm, and mould the form of the body.

The flagella occupy the anterior or rounded end of the trichomonad. Although Dock determined in the *Trichomonas hominis vaginalis* four distinct flagella, their number in the *T. intestinalis* has been variously given. I have examined a large number of trichomonads to determine the number of flagella, using freshly passed specimens of feces from each of my cases each time. I have never seen an active, normal-appearing organism with more or less than four flagella. While watching an

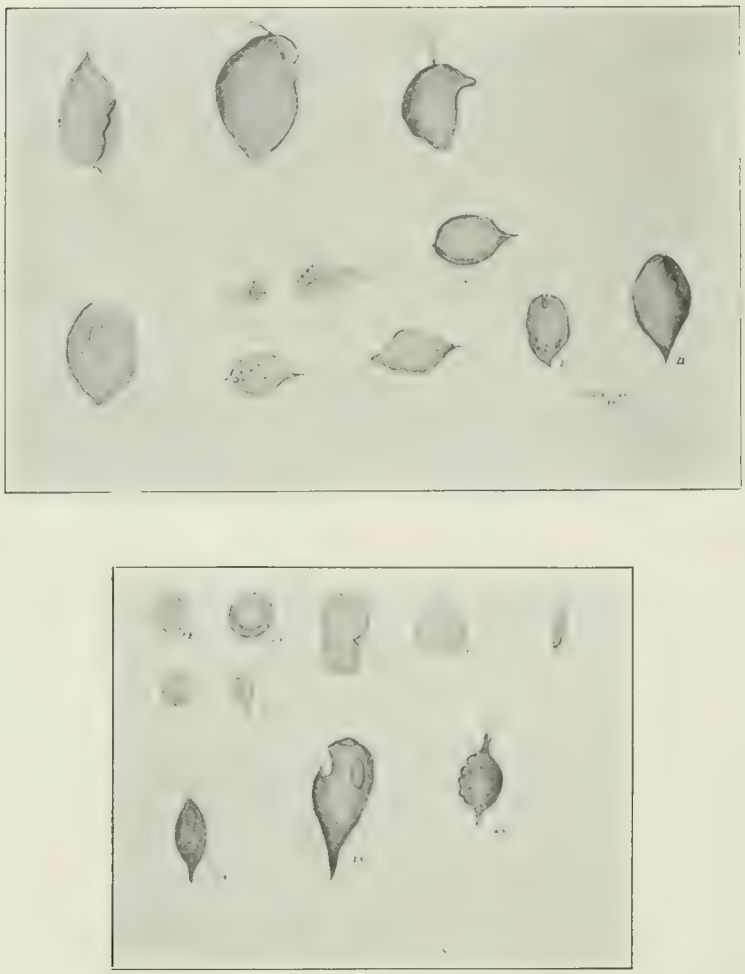

Fig. 1. — 1, 2, 3 and 4, trichomonads from bladder (after Dock) stained with methylene blue; 5 and 6, parasite from typhoid stool (after Marchand); 7, after Grassi; 8, after Zunker; 9, after May; 10, after Roos (Marchand's parasite); 11, after Roos (Davaine's parasite); 12, cyst (after May); 12-a, 13 and 14, cyst forms (after Roos); 15, 16 and 17, Lambl's parasites; 18, cimænomonas (Grassi); 19, monocercomonas (Epstein); 20, cercomonas coli hominis (May).

Fig. 2.—Trichomonads. 1, longitudinal division; 2, cyst; 3, 5, 8 and 9, normal trichomonad; 4, spore form; 6 and 7, dead trichomonads.

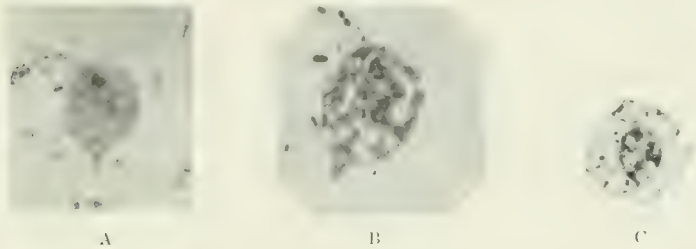

Fig. 3.—Stained trichomonads. A, ×1380; B, ×1500; C, ×830.

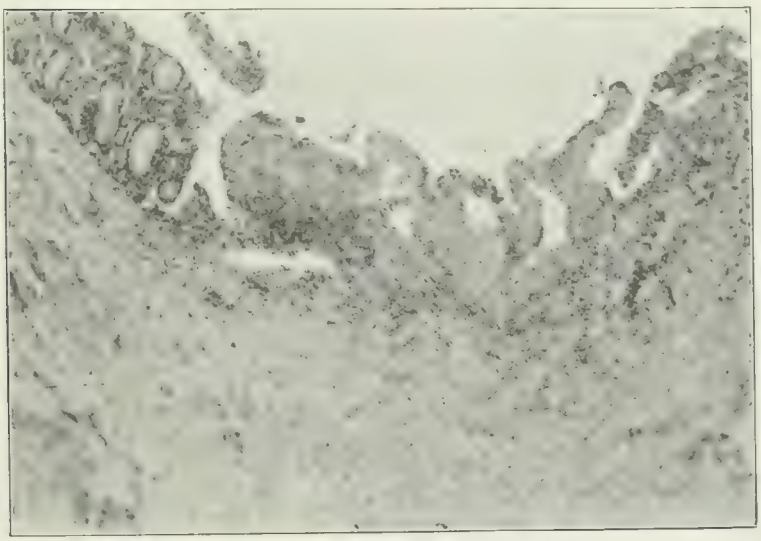

Fig. 4.—Ulcer from colon, ×48.

organism, I have frequently seen it lose one, two, three and even all its flagella. I have seen them become intertwined, giving the appearance of one or two thick flagella, or they have become inactive and dropped alongside of the cell out of focus. I am firmly convinced, however, that every normal trichomonad is possessed of four of these slender lashes at some time during its existence. The flagella spring not from a single point, as some have said, and the remainder taken for granted, but from a small elevated area at the anterior end. Marchand described a rostrum from which they arose. In this I partly agree with him. In the lateral view, in which we see most of the forms, an old and slowly moving form will show the bases of three in a row, the center the most prominent, the two lateral a trifle out of focus. The fourth is invisible, because its origin is opposite the middle flagellum. The ectoplasm at the point of emergence of the flagella is thicker, forming a slight projection. An anterior view shows four distinct points of origin, especially when each flagellum is everted (see drawings). The length of the flagella is variable. They average about nine microns. Roughly, they are as long as the body of the trichomonad itself. They are about one-fourth micron in thickness, and of the same breadth at the tip as at the base. Their ends are rounded. They are homogeneous and impart the same shimmering appearance as does the remainder of the ectoplasm.

Extending backward along the body of the trichomonad in an oblique or curved line from the base of the flagella, to and continuous with the tail, runs the undulating membrane. Its free border is longer than its line of origin. Consequently it lies in folds, giving it an escalloped and plaited effect, which, when active, shows waves running anteriorly and posteriorly. Early it was taken for a row of cilia of varying length. Many of the recent writers describe it as running from one-half to two-thirds the length of the cell. It is seen with difficulty when at rest. Its course is best followed when the organism is moving slowly. When but slightly developed, as in the younger form, it resembles a short fin, occupying only the anterior third or less. During the life of the few organisms that I have been able to follow, however, the entire membrane has been visible at some time during its existence. On the other hand, I have seen a fully developed membrane become rapidly smaller as if some contractile power of the ectoplasm lessened its length and breadth. In older forms the membrane becomes lax and loses some of its high state of contractility. This can frequently be seen in the pseudopodia that are projected. These come from the membrane, but I have seen them in a few specimens as projections of the ectosarc itself. There is never any inclusion of the endosarc in these protrusions. Hence I am in-

clined to regard them as an evidence of oncoming dissolution and not of a physiologic function, such as is seen when the organism puts forth a portion of its entire protoplasm.

The tail of the trichomonad, structurally, resembles and is a part of the undulating membrane. It varies in size from a tiny protrusion to a well-marked appendage. The longest measured a trifle over 6 microns. It is conical in form and tapers down to a fine filament in most cases. In fewer instances it has a blunt end. At times it is absent, and, though I have never seen it absent from all the organisms for days at a time (as Dock saw in *Trichomonas vaginalis*), I have seen many examples in which the caudal end was perfectly round, with neither vestige of the old nor sign of the new tail.

The endosarc is the granular inner portion of the protoplasm and is composed of two parts. The hyaloplasm in the normal organism has a pale, grayish green shimmer. Scattered through it are many fine granules, with a few coarser, irregular masses in the central portion. Contracting vacuoles, though described by some, have never been met with in any of my specimens. Just prior to death vacuoles of all sizes are numerous, these coalescing after death to form one or more larger clear areas in the protoplasm. The nucleus, which is from one-fifth to one-sixth the size of the body, is situated in the anterior or rounded end of the trichomonad, a short distance posterior to the flagella. It is usually oval, with its long axis obliquely placed. The nucleus is surrounded by a distinct nuclear membrane. It is composed of coarse chromatin masses and contains, in most instances, a distinct nucleolus. When treated with corrosives or fixatives, the nucleus becomes more distinct and globular. The nucleolus is then seen as a dark elongated mass.

An alimentary canal has been ascribed to the trichomonad by some observers. Davaine claims to have seen an oral cavity near the anterior end. Künstler described an alimentary canal consisting of a mouth and gullet. Others were unable to find it. Epstein, though he claims to have seen a mouth opening at the anterior end, admits he never say a trichomonad engulf food. Bouchard says there is a mouth a little beyond the base of the flagella. It gives access for a tube of a definite length, terminating in granular protoplasm in which one can see many small colorless vacuoles. Dock speaks of a "shallow depression or cleft near the insertion of the flagella, which no doubt has the function of the mouth." He admits that it is uncommon. There is no doubt about the presence of a small depression near the flagella. This I have considered to be part of the undulating membrane dipping down before its first wave appears. It can be seen when the body is turned at such an angle that

this trough in the membrane assumes the appearance of a depression or cup. I have seen no esophagus nor granules or vacuoles at the base, as described by Bouchard. The manner in which the trichomonad gets its nutrition has been variously explained. It is possible that a pseudopodial action assists in engulfing minute particles and bacteria. Or there may be a set of minute openings whereby pabulum can be drawn into the cell body. The only other method is by a process of absorption and osmosis whereby the nutrient substances are continuously being taken directly into the organism. Aided by its flagella (which set up a vortex that swirls toward its body) and undulating membrane, an ever-changing current sweeps about the trichomonad. I have never seen bacterial or other inclusions, nor have any observers given positive proof of seeing such organisms in the act of feeding.

Before taking up the additional features disclosed in the stained specimen, a short description of the various methods employed to stain these organisms will be necessary. Litten first succeeded with a combination of eosin and methyl violet. All but the nucleus was stained. Streng, in working with the infusoria that he found in cases of lung gangrene, was unable to stain them, but found that Lugol's solution brought out their flagella. Dock and Janowski, in 1896, experimented with many reagents and dyes. The former found that staining living specimens or specimens recently killed with weak corrosive sublimate gave the most satisfactory results. All the other fixatives worked poorly. Bichlorid of mercury kills the organism instantly, but produces changes in the protoplasm that alter the true picture. Staining with methylene blue destroys the protoplasm still further and increases the number of artefacts that have sometimes been described as exceptional characteristics of the trichomonad. Acetic carmine may be employed to bring out the nucleus with good effects. The nuclear membrane, which is made especially distinct by this method, has been questioned by some observers. Galli-Valerio has used carbolic fuchsin with excellent results. Prowazek used neutral red, a dye that had previously been considered inferior by other workers. He states that in one specimen he found fourteen cocci in a cell. Ucke, in 1903, employed thionin-eosin. The nucleus stained red by this method, and better differentiation was obtained than with any previous method. Krause, in 1906, used May-Grünwald, staining but one specimen at all satisfactorily. This one good result with a triple stain was proof positive to me that by modifying our methods success must eventually follow its use.

The trichomonad has several peculiar properties. It disintegrates immediately on death of the organism and drying kills at once. There-

fore, to stain the parasite of the intestinal tract, immediate staining, following quick fixation, are the requirements that must be fulfilled. It is first necessary to mix some thin fixative with the stool rich in trichomonads. Egg albumin suffices. Drying a thin, rapidly spread film with the aid of a moderate degree of heat is best. I employed almost every kind of fixative—heat, absolute alcohol, methyl alcohol, ether and alcohol, osmic acid, corrosive sublimate and formalin. Of these, none gave more unqualified satisfaction than the fumes of 1 per cent. osmic acid followed at once by one of the polychrome dyes in a solution of methyl alcohol. I used Romanowski, modified Romanowski, Wright, Giemsa and MacNeal mixtures, all modifications of the polychrome stains. Wright's stain gave the best results, because I was more accustomed to manipulating it and because of the rapidity of its action. In this manner I was able to obtain stained specimens of the trichomonad, staining differentially the nucleus, protoplasm and appendages. I have been unable thus far to stain an organism in its normal form. As the drawings and photographs indicate, they become globular, a few remaining pyriform. This is readily explained. The moderate warmth and rapid drying of the film does not kill the organism, as can be demonstrated by quickly examining such a partially fixed specimen with a one-seventh objective. The organism has lost some of its activity, however. Then follows immediate fixation and drying with the fumes of osmic acid. The alcohol of Wright's stain further fixes the trichomonad, so that it is stained in that form.

Examination of the stained specimen reveals new facts. The protoplasm is dyed a deep blue and contains a few irregular vacuoles due, no doubt, to fixation. The nucleus occupying the anterior portion of the cell is stained deeply by methylene red, the chromatin resembling closely the nuclear material of a malarial parasite. It is dense, closely packed, and occasionally a darker area situated to one side suggests a nucleolus. The appendages are very pale. The undulating membrane can be seen in relatively few instances. It stains a grayish pink and continues into the tail, which stains a similar color. The tail tapers off gradually, sometimes extending out into a long thin filament. Anteriorly the flagella appear as pale, drab-colored, fine filaments springing from the ectoplasm as it is seen extending forward from the membrane. They lie close alongside of the body wall.

The trichomonad is one of the most actively motile of the monocellular parasites. It has three different kinds of motion. The first is quick and jerky and has no constant direction. The second is due to the activity of the appendages and by its aid the organism swims about.

The third is pseudopodial. The trichomonad not only employs its flagella, undulating membrane and tail, but the natural contractility of the protoplasm is perpetually altering the shape and position of the organism in the field. This power, I believe, lies in the ectoplasm mainly, and acts in conjunction with the appendages. Of these the flagella are the most active. When the organism is at rest, they float in wide curves in front of or at the side of the cell body. But when motion begins they start from the extended position and sweep down the body of the trichomonad in a snapping, whip-like manner. They alter this motion frequently in that two act together on one side, or one or more remain inactive. It is in this way that the flagella, flapping against the side of the organism, set up currents that aid in propelling it forward. As each contraction beginning in the flagella sets up its wave, it simultaneously transmits this wave to the undulating membrane. Thus the wave travels from the anterior pole of the cell quickly backward in from three to six undulations into the tail. These waves, started in rapid succession, keep up incessantly, and give the membrane an appearance not unlike flowing water. The undulating membrane has several purposes. It keeps an ever-changing current of fluid about the body; it acts as an organ of locomotion in a small degree, and serves as a keel at times. The tail takes an active part in locomotion. Both by virtue of its long tapering end and its power it forms the most active organ of propulsion. This is especially borne out by the diminished activity in those forms that have lost their tails.

The trichomonad has a further function (described by Marchand in 1875), that of putting forth pseudopodia. This process differs from the prolongations of the ectoplasm previously described. It occurs but rarely in the intestinalis, though it is often seen in the vaginalis. The pseudopod consists of a prolongation of both the ectoplasm and the endoplasm. It is protruded slowly and usually remains as a projected part of the protoplasm for some time. It does not have the flowing motion as is seen typically in the ameba, and it retracts again very slowly. Prowazek has observed these protrusions in the *Trichomonas laceratæ*. In his instances the nucleus, undulating membrane and flagella divided before the protoplasm was finally constricted. He believed it to be a process of direct division. Dock described some very pretty examples and ascribed the function of pseudopodial formation to that of nutrition. I have sought diligently and have seen but an occasional poor specimen in an old cell. These organisms soon died, so that I can neither affirm nor deny the views of either observers as to the function of the pseudopod.

The trichomonad is susceptible not only to chemical reagents, but heat and cold also markedly influence it. It can live in slightly acid, neutral or alkaline media. Heat of 45 degrees C. quickly kills the organism. Cold has the same effect in that the organism lives but one-half hour at 20 degrees C. The longest I have ever been able to keep any alive and active on a warming stage has been forty-two hours. Placing some of the infected material in an incubator, a few sluggish forms could be detected at the end of sixty-six hours. Unlike amebæ, these organisms do not respond to the slight heating of the slide on which they are spread after their motility has once diminished. The first sign of oncoming death of the trichomonad is a lowered motility, especially in the short, quick, characteristic jerky movements. Then follows a lessening in the activity of the appendages. The flagella are seen in any position waving irregularly. The undulating membrane becomes more distinct and its waves are slower. The tail ceases motion, too. The body assumes a more globular shape and masses of the protoplasm heap together to form darkened areas. Vacuoles appear in contrast. These soon coalesce to form larger, clearer areas. Soon the membrane disappears, together with the tail and the flagella. The cell becomes darker, denser and more globular. Suddenly it plasmolyzes and seldom a vestige of the cell remains.

It is impossible to cultivate these organisms. Growth under anaërobic conditions has so frequently failed that I made no further attempts. I tried, however, a process of fishing for these organisms with a fine platinum wire under a one-fourth power objective, and transplanted them to a culture medium of coli communis of *proteus vulgaris*, and of the mixed growth. I incubated two, six and ten hours. I was unable to find them afterward in any instance. Then I tried to transplant them to the mucosa of the gut of a sheep and of a pig by transferring loopfuls of fecal material rich in trichomonads to the partly cleansed gut of these animals, kept in a moist chamber at body heat. Here, too, my parasites died. Finally, I endeavored to infect the alimentary tracts of numerous animals, employing the cat, dog, rabbit and guinea-pig. I injected small amounts per rectum and also mixed fresh material with their food at various times. No diarrhea resulted, nor could I find trichomonads in the subsequent passages of these animals.

The important question now arises as to how these parasites reproduce if they are so short lived outside of the human body and no trace is left of them after death. It has long been known that direct division is common among all monocellular organisms. Monocellular parasites also have the power, after passing through a definite cycle, of forming bodies

more resistant than themselves that are readily disseminated, and capable in proper soil of forming new adult organisms. The flagellated are not the lowest in the scale possessing this power of reproduction and propagation. They possess both the power of direct cleavage and cyclical division or "spore building." It is not uncommon to see splitting take place in the trichomonad. Fresh specimens, on a warming stage, frequently show forms in different degrees of division. Lambl, in 1859, probably was the first to see dividing occur, though his description is vague. Pfeiffer, Künstler, Cunningham, Bouchard, Marchand and other observers describe division quite accurately, they having seen it take place in specimens from the stool, urine and vagina. It occurs with varying frequency. The cleavage is longitudinal, there being equal splitting of the undulating membrane, as well as of the flagella, tail, nucleus and body.* It requires from forty minutes to one and one-half hours for complete division to take place. As soon as the parasites have become partially divided, a continual tugging motion is set up until finally they split into two small active forms and swim away rapidly.

Though much doubt exists in the minds of many investigators as to the existence of a definite cycle, the formation of cysts or spores has been quite generally observed. Nothnagel, in 1881, so far as I can determine, first described cyst forms or "Dauer-sporen." He thought they were dead monads. Perroncito, in 1887, claims to have seen cyst formation. The trichomonad dropped its flagella and tail, became globular, and a dark exterior and a light interior became differentiated. Roos, in 1893, speaks of encysted forms that appeared in one of his cases when the stool was free from motile forms. These were small, round, refractive, greenish bodies, sharply outlined, immobile and with no inner structure. They varied from 5.5 to 7.5 microns in diameter. He also saw larger bodies, 14 to 17 microns, with distinct cell contour or double membrane, containing small, round, greenish bodies. These were found on various occasions in the stools.

Contrary to these observations, Schmidt and Strassburger claim that cysts are not known. Epstein saw neither division nor cysts. Dock, though never having observed such forms, admits their possibility, saying, "it seems there must be some other method of reproduction than that by division." In recent years several workers have seen spore bodies. Galli-Valerio saw cysts in a patient in which trichomonads were found in a cancer of the jaw. Theobald had a similar case. Ucke demonstrated that besides ordinary encysted forms, stages could be made out

* Prowazek has noted a division into three in a form *Trichomonas lacerata* closely resembling and allied to the *Trichomonas hominis intestinalis.*

in cyst formation. In changing to the encysted form he saw the trichomonad lose all its appendages and become round and later become oval again. I have frequently seen cysts in all the cases that I had the opportunity to examine. I have never seen similar bodies in non-infected feces. They appear in increasing number, a few being seen one day, a great many the next, and the number then diminishing till no more are seen. Their appearance is not periodic. Contrary to some earlier observers, a cyst does not imply a single encapsulated trichomonad capable of resisting severe influences and evolved solely for the preservation of the species. A cyst is a heavily encapsulated body containing two or more (up to twenty) small pale, greenish, shimmering spores about a central mass of cellular material, capable of spreading after rupture of the wall. From these small spores the adult trichomonad finally develops.

Just what causes the trichomonad to undergo cyst formation has been in doubt. Whether copulation takes place or not, only continued observations can determine. Schaudinn, in 1903, mentions the union of two parasites. Previous to copulation the organisms lost their flagella and moved about by pseudopods. They united and their nuclei underwent several reductions from which cysts resulted. Krause last year described propagation of the trichomonad by copulation. Usually a larger form seized a smaller one, during which the flagella were intertwined, thus uniting the organisms by their anterior ends. After several efforts on the part of the smaller form to separate from the larger, the two remained together from three to six minutes, moving actively all the while. The nucleus gradually sought the periphera and showed lively motion in its center. After several futile attempts the smaller tore itself from the larger and slowly moved away. The larger, meanwhile, showed unusually energetic motion. Here his description ends, no further mention being made of what became of either form. This observation of Krause I can substantiate by several that I have had the good fortune to witness in my cases. I have not seen the approach of the nucleus to the periphera, nor have I seen any interchange of nuclear material. The changes that took place after the separation of the two forms interested me mostly, in that the formation of cysts was thereby explained.

I was able to observe one specimen on the warming stage in which two organisms, one smaller and one larger, united by their anterior ends. After active tussling motions for about four minutes, during which time both lost their tails and undulating membranes, the two forms separated, the smaller one floating to one side and the larger remaining quite active in the field. This motion presently became less,

when darker masses of protoplasm could be seen dancing throughout the cell. These soon collected in the middle, the outer part being taken up by globular, highly refracting greenish bodies. The cell was now motionless. The membrane was distinctly double. There was a small indentation at one edge, but I could not determine its nature. I have seen similar notches in many specimens since. With the view of determining what would become of the cyst, I watched it for six hours without noting any changes in its shape, size or activity. Cold water was run through the chamber of the stage without any effect. While allowing hot water to flow through I accidentally lost this cell. Since then I have applied heat to similar bodies. The first action is to cause them to swell up. Suddenly the membrane breaks and many little spores are set free. These soon die, probably from the effect of the heat. I have observed, from time to time, however, in infected stools, the presence of small, round, highly-refracting bodies with a single flagellum. They are from 4 to 7.5 microns in diameter and move about fairly rapidly. I have watched these for hours, but have never been able to keep them alive long enough to observe any other change in them but a decided growth and partial elongation. They suggest to me, however, young spores that have become active.

This brings to mind an observation of May, made in 1892. He is certain that on the warming stage smaller forms with one flagellum and rapid ameboid movement are transformed into adult trichomonads. Their bodies lengthen to form a tapering end; projections of the protoplasm slowly appear, following which they take on a more rapid motion. Gradually an undulating membrane forms and suddenly flagella appear. May adds that he did not see the reverse take place. Whether the foregoing observations are the fragmentary evidence of a sexual cycle, diligent and accurate work in these forms will alone determine.

During my studies on the trichomonad I had the opportunity of observing the clinical course and symptoms of ten cases in which these organisms were discovered in the feces. These patients came with a variety of complaints, some relating solely to intestinal disturbances, others presenting the picture of some organic disease. A short outline of each of these cases will be given for the purpose of determining, if possible, the influence of the trichomonad as a causative factor in enteritis.

CASE 1.—The first case of this kind was in a male, aged 42, a photographer, who came to the medical clinic complaining of weakness on exertion, shortness of breath, pallor and diarrhea with watery stools. His father died of "bowel trouble"

after one day's illness. His mother died of "nosebleed." No other history of importance was obtainable. Eighteen months previous to his admission (Jan. 26, 1906) the patient began to notice a change in his color and some loss of weight. In twelve months he lost sixty pounds. Three months ago his appetite began to fail him and weakness on the least exertion became pronounced. The swelling of his ankles has been recent. The diarrhea is of six months' standing. The passages are not frequent, but are thin and watery at times. He has noticed "slime" in his stools, but never any blood. No tarry stools. There is a slight, constant pain in the rectum, but never any tenesmus. He has had intervals of cramping pain radiating all over the abdomen. At these times he did not note any exacerbation of the intestinal symptoms.

The important features of the physical examination were the weak, flabby muscles, the lemon-colored, wax-like skin, the extremely pale mucous membranes, the bluish tinted sclerotics and the moderate edema of the lower extremities.

Spleen, liver and kidneys not palpated. Rectal examinations showed a few small hemorrhoids, but no ulceration of any kind. The mucosa was very pale.

As the blood examination showed, the patient was suffering from pernicious anemia in a severe form, red blood corpuscles 992,000, leucocytes 2,150, hemoglobin 23 per cent. A differential count gave 34.9 per cent. of small lymphocytes, 1.8 per cent. of large lymphocytes, 3 per cent. of transitionals, 62.7 per cent. of polynuclear neutrophiles, 3 per cent. of mast cells. There were many microcytes, macrocytes and poikilocytes. One megaloblast and eight stipple cells were seen.

The urine on admission was acid, dark reddish yellow, 1.014; no albumin: no sugar; no bile. A strong test for indican was present. The white, flocculent sediment was composed of leucocytes, a few squamous cells and bacteria.

Test meals revealed achlorhydria, apepsia, a rapid motility, and a slight excess of mucus.

The stool examined on February 2 was as follows: About one-half pint of light brown stool of creamy consistency, containing small flakes of mucus; no macroscopic blood nor food particles. Occult blood tests were negative. Microscopically, many triple phosphate crystals; no Charcot crystals; some vegetable and some muscle fibers. A large number of trichomonads and many cells, from four to six times the diameter of a red blood cell, showing a clear, hyaline, outer margin and numerous small round vacuoles were present. Some of them have brownish pigment, but none have red blood cells in them. No red blood cells were seen in the spread; many leucocytes and small epithelial cells; bacteria very numerous.

The patient was given small salines daily, followed in an hour by a liter of warm water containing fifteen grains of quinin sulphate. The patient had some difficulty in retaining these enemas, and they were later discontinued. Hydrochloric acid, twenty-five drops, after meals, and "anemic" diet were ordered.

The patient did not show any perceptible improvement. The progressive anemia could not be checked. Some of the more important data in his case are given below.

February 7.—Patient had six stools yesterday. The general character has been light brown fluid and with a distinct dysenteric odor. There has been much mucus. All contain ameba coli and trichomonads, the latter in great numbers. They vary in size from 6 to 12 microns in body length, with long tapering tails. In one field six bean-shaped bodies are seen, measuring 10 by 12 microns, nonmotile, and containing many small granular bodies and a single vacuole. They resemble spore bodies.

February 11.—The patient showed some slight improvement, gaining both in strength and in appetite. The blood examination was in all respects the same as

at the first. The number of his stools became fewer from that time on, the trichomonads being less numerous and the mucus disappearing.

February 21.—The patient complained of feeling chilly this afternoon. He had a slight rise of temperature, which later rose to 103.2.

Stool Examination.—There are many live actively motile ameba. There are two types of trichomonads. A larger type described before and a smaller form measuring from 3 to 5 microns. These small organisms show different motions than the larger ones. They possess quick, jerky, protoplasmic motions, running first in one direction and then in another. They have two flagella. The nucleus is in the center of the cell. There is no undulating membrane. These trichomonads were in excess in the stool at 2 p. m. At 5 p. m. but few of the larger ones were to be seen. In the last passage all forms are absent.

The patient's rise in temperature continued. He became much weaker, the stools were on an average of four a day and contained many parasites of all types. On the 24th the red blood cells numbered 744.000; white cells, 2,000; hemoglobin, 9 per cent. (?). Differential count showed 53.8 per cent. of small lymphocytes and 45.8 per cent. of polynuclear leucocytes. There were many misshapen cells, 13 megaloblasts in 500 cells counted, a few stipple cells and much polychromatophilia.

On the 26th the patient had a severe nosebleed requiring plugging of the left nares. This loss of blood did not cause any marked change in the blood count. About this time a diffuse swelling appeared about both eyes that was at first taken for edema. The following day it was noticed that this spread in all directions on the face, with a slight line of demarcation. There was no redness and only a moderate amount of induration and tenderness. There was no rise in the leucocyte count, but the differential count showed a marked rise in the polynuclear forms.

The patient gradually became weaker. He had numerous attacks of epistaxis. His stools were more frequent, and soon were passed involuntarily. His heart weakened suddenly, and on March 4 he died. An autopsy was performed by Prof. A. S. Warthin, to whom I am indebted for the notes and specimens.

The pathologic diagnosis is all that will be necessary in this case. There was progressive pernicious anemia; hyperplasia of bone marrow, pulp of spleen and hemolymph nodes; hemosiderosis of spleen, liver and hemolymph nodes. Lobular, fibrinous pneumonia of the left lung. Congestion and edema of the right lung. Cloudy swelling and fatty degeneration of heart muscles, liver and kidneys. Central zone of necrosis of liver.

Stomach small, contains small amount of yellow-gray fluid of sour odor. Tenacious mucus covers the atrophic mucosa. Small intestine contains slight amount of light-yellow, semi-fluid, tenacious material; considerable edema of submucous tissue. Muscular coat is thin. Marked congestion of caput coli. Large intestine: many small bits of mucus, many of them blood-stained. Walls very thin in upper two-thirds. There are numerous superficial ulcers, irregular, circular and oval in outline. The margins are raised. The bases are smooth, consisting of whitish granular material, 4x6 mms. in diameter. Lower one-third free from ulceration.

On microscopic examination of fresh material from different portions of the intestine trichomonads were found, chiefly in the small gut and mostly in the upper portion. There were some in the large intestine, especially in the granular detritus covering the erosions. Some amebæ were present throughout the entire tract. The mucosa of the stomach showed slight round-celled infiltration. No atrophy. The mucosa of the ileum was slightly atrophic. The epithelium of the mucous lining of the colon was absent. There was round-celled infiltration. Typical small ulcers. Some hyperplasia of connective tissues about the ulcers.

CASE 2.—The second patient came to the medical clinic June 2, 1906. This patient was aged 35, single, an engineer by occupation. His illness began with cramping pains in the abdomen, dull headache, and malaise. The patient lost his appetite and was nauseated at times. From this he slowly recovered. Three weeks later he was seized with severe pains in the right side, at the margin of the ribs, which radiated over the entire abdomen. The pains were periodic. No vomiting and no jaundice at any time. Stools were yellow and had a sour odor. There were from three to five movements daily. The patient weakened very rapidly and was unable to move about without assistance. At this time the patient was brought to the University Hospital. Abdomen was on the level of the ribs, lax, with peristaltic movements clearly visible. No painful points, but a diffuse tenderness on superficial as well as deep palpation. Spleen, liver and kidneys not palpable. Rectum negative.

Urine: Specific gravity, 1,024; acid and reddish brown in color. No albumin; no sugar; no bile; indican in large amounts; no diazo reaction; sediment small, composed mostly of urates.

Blood: Red blood corpuscles, 3,550,000; leucocytes, 11,240; hemoglobin, 80 per cent.; Widal reaction negative.

Stool: Medium sized, light brownish yellow, with a distinctly putrid odor. Faint occult blood reaction obtained. No macroscopic blood. Small bits of mucus, in which are found large numbers of actively motile trichomonads. Some undigested starch.

The patient's condition remained about the same. He had slight, daily rise of temperature in the afternoon, occasionally reaching 102.5. The soreness in the abdomen persisted, the stools continuing to have all the characteristics described above. The blood appeared at times while the patient was on a strict diet. He became steadily more anemic, however. He lost nine pounds the first week in the hospital, and continued to lose for the following three weeks. The patient was then put on frequent, small doses of salol, and was given cool enemata. His diet was light, and he was kept in bed and out of doors most of the time. About July 1 the pains disappeared and he became brighter. His appetite improved, and the movements became natural. The trichomonads were present, but in much fewer numbers, being absent for days at a time. He left the hospital with instructions to continue treatment, fresh air and rest. He gained in weight up to 160 pounds, returning to his work in October. He has had two periods since when he experienced attacks of constipation alternating with diarrhea, with cramping pains in the abdomen, lasting, in all, one week. At these times he describes the stools as being of the same gross appearance as those he passed during his initial illness.

CASE 3.—J. H. B., aged 62, farmer, came to the medical clinic Nov. 11, 1906, complaining of colicky pains in the abdomen, and diarrhea. At the age of 18 the patient went to war and served in the Union army for a period of two years. The diarrhea, of which he complains now, began during his service while in Tennessee. All the men in the ranks had attacks of what the physicians of the regiments then called "mild cholera morbus." They assigned this to the water, which was often procured from pools and ponds. The diarrhea which he experienced in the service was accompanied with some sharp, griping pains, but how long these lasted he does not remember, for he was wounded soon after.

He has had repeated attacks of diarrhea ever since. These come from twice to three times a year, and last for a month or six weeks. In 1892 the patient had a very severe attack, of short duration, during which excruciating, cramping pains in the abdomen and very frequent passages kept him confined to bed for two weeks. He lost in weight and strength at this time. Subsequent attacks were less severe until 1902, when gastric distress complicated the diarrhea, which grew

worse in proportion. The present attack began about four weeks ago and the patient is about recovering from it at the present time. He has had from five to six stools a day, very loose and watery, not of a very offensive odor, but apparently containing much undigested food. At the height of the present illness the patient had from fifteen to sixteen stools during the day, with incontinence of feces at night. There were some pains of a colicky nature, but these have subsided. He passes little or no gas. No pain with defecation. During this last attack the stomach symptoms became aggravated. The distress in the epigastrium, of which he complains, is relieved, however, by going to stool. Physical examination is negative.

Blood: Red blood corpuscles, 5,240,000; leucocytes, 6,170; hemoglobin, 100 per cent. Of 615 white cells counted, 14.3 per cent. were small lymphocytes, 13.1 per cent. were large lymphocytes, .3 per cent. transitionals, 65.2 per cent. polynuclears, 2 per cent. eosinophiles, 1.1 per cent. mast cells, and 4.1 per cent. degenerates and undetermined cells.

Urine: The twenty-four hour amount was scanty. The specific gravity was never below 1,021. Acid; no albumin; no sugar; moderate sediment of urates at times. There was always a strong reaction for indican.

Stomach: The patient's stomach showed a lack of free hydrochloric acid, at times, and a diminution in the ferments. There was an increase in the motor power, with an excess of mucus and the presence of non-motile rods and cocci at each examination.

The patient was put on an intestinal test diet at once, and his stools were examined. The first day he had five passages. The stools were thin, light yellow, and granular. No macroscopic food remains. Microscopic examination of small bits of thin mucus revealed a large number of active trichomonads with some round, less motile and darker bodies. Occult test negative. The patient was then given a large dose of Carlsbad salts, which was followed the next day by one very large stool and two smaller ones. Enormous numbers of trichomonads were found. No blood. The third day he had four passages, the trichomonads being still quite numerous. In the last passage, however, there were fewer than there had been at any time since his admission. The remaining four days that the patient was in the hospital he had but one thick and unformed passage each day. The trichomonads were present, but in very much smaller numbers than before. The griping had disappeared and the patient's strength returned. He was sent home and advised to take saline cathartics twice a week, following repeated small doses of calomel. He has had no attack since.

Case 4.—G. C. presented himself to the medical clinic complaining of pain in the "stomach" and "bowels" and a violent headache. He dated his present illness to four years previously when he had a similar attack. At that time he had severe abdominal pain and diarrhea. He had about twelve passages the first day; after that they became fewer. He kept about for a couple of days, but his fever rose to 105, so he went to bed, where he remained for three weeks. During this time he had severe continued pain in the lower abdomen and some fever. He improved for a while, but while working in a lumber camp the intestinal trouble became so severe that he was obliged to discontinue his heavy work. In the fall of 1903 he was ill for three months again with "bowel trouble," with severe pain and constipation. Since then he has had difficulty in securing a daily movement. The fall of 1906 found the patient suffering much more pain all over the abdomen, but no diarrhea.

The present attack came on two weeks before admission to the clinic. He had suffered from diarrhea, after which his strength failed and he lost weight. There has been continual soreness and distress in his abdomen. He has had some slight nose-bleed of late. The severe headache has persisted for the past two days. The

patient has a tired expression. He protrudes his tongue, which is red, swollen, and heavily coated, very slowly. Breathing is accelerated and somewhat labored. Pulse small, low tension, regular rate 108, temperature 102. Percussion of the lungs was negative. A harsh vesicular breathing with râles could be heard all over the upper portion of the thorax. Heart not enlarged; sounds clear and of moderate intensity. The abdomen is below the level of the ribs; walls are moderately relaxed, and the spleen is just felt on deep breathing. There is some tenderness on palpation in the right iliac fossa. No rosella over trunk.

There was the suspicion of a more acute and recent infection. Examination of the urine gave a strong diazo reaction, and the following day the positive Widal assured us of the diagnosis of typhoid fever. The patient was given 5 grains of calomel, followed by salts. In the stools were found numerous trichomonads. The patient became more diarrheic as the typhoid fever progressed. Trichomonads were seldom seen in these frequent passages. At one time, however, many cyst forms were observed. No active parasites were present at this time, nor did they appear till three days later. Blood, due to the typhoid hemorrhage, was present on several occasions. Cholecystitis further complicated the course of the case.

At present the patient is well and about. His diarrhea abated with his convalescence. He still has two movements a day, as a rule. The feces are soft, light yellow in color, and contain a small number of trichomonads. He has not been constipated. The patient now states that he does not remember having been obliged to drink water that could have been considered stagnant or impure at any time previous to his first attack of pain and diarrhea.

Case 5.—R. E. was referred from the surgical clinic for examination concerning pain in the right hypochondrium which spread over the entire abdomen. The patient was a male, aged 24, a day laborer by occupation. He had never had any previous illness. Three years previous he had an attack of "appendicitis." Following this the pain became constant. In the summer of 1905, appendectomy was performed at another hospital. The pain did not subside, however. At present he has aching and cramping pains in the right side which come on in the afternoon and last until midnight. They spread over the entire abdomen. Eating does not affect the pains. The patient vomits at times, but the vomitus has never looked black, nor has there ever been blood in the vomitus. No history of jaundice or clay-colored stools. No tarry stools. The patient has lost some weight. Heart and lungs are normal. Abdomen is below the level of the ribs. Spleen, liver, and kidneys not palpable. In a later examination, large peristaltic movements are seen in the epigastrium traveling from left to right. On distension of the stomach, no enlargement is noted. No pain. There is some pain and tenderness at the level of the eighth dorsal vertebra on the right side. At this time the patient was having on an average four stools a day.

Blood examination: 3,650,000 red cells, 7,000 white cells, 45 per cent. hemoglobin. Differential count shows no alteration in relative count.

Urine examination: Negative.

Test meals revealed a normal acidity, a lowered motility, an excess of mucus at times, normal amount of pepsin and chymosin. The stomach was neither enlarged nor prolapsed.

The stools on several examinations were pale brown in color and of creamy consistency. No undigested food remains. No blood. Occult blood test negative. Microscopically, large numbers of trichomonads were seen. They were very active and could be kept alive in the stool for ten hours at room temperature. No blood cells nor leucocytes seen. Four days after admission the morning passage gave a positive test for blood. Blood cells not seen.

As an exploratory operation was desired by the surgical clinic, the patient was put at rest, given a special diet, and Blaud's pills, in increasing doses, were administered. For the paroxysms of pain, morphin was given. The blood count improved considerably so that at the end of a week the red cells numbered 3,984,000, and the hemoglobin percentage was 70.

The patient had fewer passages, as was to be expected, but the stool was still soft and contained enormous numbers of trichomonads. An operation was deemed inadvisable at this time, and the patient, refusing to stay for further medical treatment, left the hospital. His subsequent course is not known.

CASE 6.—B. E. P. was admitted to the medical clinic Dec. 19, 1906, complaining of numbness, distress in the stomach and diarrhea. The family history is of value in one respect, in that a sister of the patient has pernicious anemia. He has been well up to the present illness, which began two years ago with loss of appetite, belching of gas and diarrhea. He vomited occasionally. In November, 1906, the numbness of which he now complains became pronounced. Ankles and feet especially felt cold; he lost both weight and strength. Recently his bowels have become constipated.

The patient is of slender build, musculature is soft and flabby. The skin is pale, dry and slightly inelastic. The tongue is furred, and the mucous membranes of the mouth are pale. Teeth are in good condition. Sclerotics are clear and of a bluish tinge. The lungs and heart are normal. The abdomen is two finger breadths below the level of the ribs. Slight tenderness in the epigastrium. Edge of the liver and the spleen can be felt on inspiration. Lymphatics not enlarged.

Blood: Red blood corpuscles, 2,464,000; leucocytes, 2,600; hemoglobin, 54 per cent. A differential count of 550 cells shows: Small lymphocytes, 42 per cent.; large lymphocytes, 16.5 per cent.; transitional, 5 per cent.; polynuclear, 40 per cent. There is much poikilocytosis; there are many megalocytes, but no megaloblasts are seen.

It is evident from the foregoing that this is another case of pernicious anemia.

About a week after the patient's admission, his bowels, which up to that time had been regular, and the feces normal and free from blood, became diarrheic. He had, at first, two partly formed passages which rose to five in a few days, and were liquid. They were yellowish brown in color, watery, and had a strong odor of hydrogen sulphid. There were a few undigested particles of meat and many starch granules. There was a small amount of mucus in fine flakes. In these particles many trichomonads were seen. No microscopic or occult blood.

The urine examination was as follows: Specific gravity, 1,025; acid reaction and reddish yellow in color. A 24-hour sample of 1,240 c.c. showed a large deposit of urates. Indican gave a deep blue reaction. No albumin; no sugar. A few fine granular short casts were seen.

The stomach examination showed an achylia, with a very rapid motility and an increase of mucus.

The patient was put on treatment for the pernicious anemia, and special attention was given to his diarrhea. The patient soon began to improve and his gain was rapid. The stools became natural and regular, and at the end of six weeks no more trichomonads were to be found. His blood picture has returned almost to normal, and at the last report the patient was enjoying good health.

CASE 7.—R. E. W., aged 31, is at present a student in the University. His family history and early history are of no importance in his case. He was a captain in the United States Marine Corps up to four years ago, and has been in all parts of the world, taking at that time no more than ordinary precautions about his food and drink. He first noticed his discomfort in the summer of 1903, while he was in Florida, where he drank from a spring the water of which he had

reason to believe was not absolutely pure. At that time the initial attack was characterized by pain in the abdomen, which began early in the morning and persisted all day. It grew worse toward noon, so that he could not be up and about. He felt better the next day. He did not vomit, had no fever and no diarrhea. The abdomen was sore for two or three days afterward. Every three months he has had similar attacks, which followed the same course. The patient says that just preceding the attacks he feels better than he has for some time before.

In the fall of 1905 he examined his stools for the first time and found *Trichocephalus dispar* ova and trichomonads in large numbers. I saw the feces soon afterward and was able to confirm these findings. I have studied the trichomonads in this patient's stools frequently, and always found them present in large numbers after the administration of a saline cathartic.

The patient later on took thymol and succeeded in ridding himself of the trichocephalus. Whether or not the trichomonads became fewer he does not know, but this drug must surely have had some effect on the organisms. He had the attacks with varying frequency up to January, 1906. He was often confined to his bed for a day or two, but at no time did he note any change in the consistency of his stools. Since the administration of thymol there have not been any very bad attacks. He had one last December which incapacitated him for one day.

On April, 8, 1907, he had the "beginning sensations" of another attack. The pain was less severe than on previous occasions, and he had no discomfort on the following day. It should be stated that during the first week in February the patient took ¼ gr. of calomel three times daily for one week.

A stool examined on April 11 showed a few trichomonads which had lively motion and all the characteristics previously noted. The number was greatly reduced to that which had been found on previous occasions on the giving of salts. No ova were seen.

The urine of the patient is normal in all respects, except for the occasional presence of indican.

Blood counts: Red blood corpuscles, 5,500,000; leucocytes, 8,000; hemoglobin, 80 per cent. The eosinophiles average at about 10 per cent., the proportion of the other cells being normal.

Case 8.—The patient, male, aged 29, farmer by occupation, came to the hospital because of diarrhea, pain of a griping nature when the bowels moved, and extreme emaciation. He was admitted April 22, 1907. The family history and personal history up to first attack of diarrhea in 1900, are good. In December, 1900, the patient was employed as a surveyor, which required him to go to many different places and drink of waters that he has every reason now to think were unclean. At this time he first noticed a diarrhea, passing at the outset a few stools a day, and later having thin and watery passages about every two hours. He had no pain and lost no weight as he remembers. He recovered in two weeks so that he could return to his work. From this time on the patient had several attacks every year, each lasting for a variable length of time. Between the attacks the patient would gain considerably in weight only to lose this again in the next attack.

In March 1907, he had an attack of "grippe." No physician attended him, but soon after he was out of bed, he suffered a relapse accompanied by diarrhea. This has persisted since, and is the longest attack from which he suffered. The bowels were at first thin and watery, light yellow, and of a foul odor. At times they have been green. No blood and no dark stools. At times there has been a small amount of mucus. No food remains as far as he has noticed. He was never constipated between the attacks.

During the last thirty days the patient has lost thirty pounds in weight, he has grown very weak, and feels nauseated most of the time. In December 1906, he weighed 140 pounds. On admission his weight was 98 pounds. Temperature 98.8; pulse 82; respirations 20.

The thorax is markedly emaciated. The lungs are normal; the heart is not enlarged, nor are the sounds abnormal. The abdomen is slightly below the navel. Abdominal walls are thin. Peristaltic movements are seen in all parts of the abdomen, especially in the lower half. No localized rigidity and no pain points. Spleen, liver and kidneys are not palpable. No enlarged glands.

Stools:—Large, thin, watery, light-brown stool of foul odor; alkaline in reaction and containing a small amount of mucus. There was a faint occult blood reaction, but no blood seen on microscopic examination. A great many actively motile trichomonads were seen. No undigested food remains; a few pus cells; no crystals.

Stomach:—Test meals show an achlorhydria, apepsia and absence of rennin. Hypermotility marked. No blood; no leucocytes; no food remains; no excess of mucus; trace of lactic present on two occasions. On one examination of the fasting stomach a few actively motile trichomonads were seen. These have not been found since. A number of cocci and bacilli were present. A bit of stomach mucosa recovered from the lavage shows a mononuclear exudate. Round ulcer(?). No evidence of malignancy.

Blood:—Red blood cells, 2,490,000; white blood cells, 5,348; hemoglobin, 55 per cent.

Urine:—Normal.

The patient was confined to bed, given very soft diet, and an astringent. After the diarrhea was checked somewhat, he was returned to a more substantial diet and calomel in 1/10 grain tablets, administered every two hours, until eight were taken daily. He was kept on this for twelve days, at which time he began to have some slight loss of appetite and nausea. The calomel was stopped and the patient returned to intestinal diet, with a bitter stomachic before meals.

An examination of the stools at this time showed them to be entirely free from trichomonads.

The patient was now permitted to go out of doors, was given a fuller diet, and iron, in the form of Blaud's pills, was administered. He improved rapidly. On May 15, he had his first formed passage. It was free from organisms and blood. He has gained steadily in weight, and now weighs 118 pounds. He is still under observation.

Case 9.—This patient, a male, student, aged 25, came to the out-patient clinic complaining of diarrhea. During the week of April 15-22, he had been out of town doing laborer's work and drinking of water that he believes was impure. On April 22 he first noticed that his stool was watery. The passages became more frequent at once, and continued in their watery character. The change came on suddenly. The bowels moved from 12 to 24 times daily. There was no griping nor pain at first, but lately there has been a little aching in the lower part of the abdomen with each defecation. The patient was given bismuth by his own physician with no relief. Later he was given a large dose of castor oil followed by salol and an astringment with no benefit. The diarrhea persisted, not quite so severe as before, but becoming worse at times. His appetite remained good. He lost some weight, and began to feel weak. He never noticed any blood, pus or food remains in the stools. They were lumpy at times and of foul odor.

The patient was a large well nourished man in good physical condition. Heart and lungs were normal. The abdomen was not tender to palpation and, except for a noticeable increased peristalsis, was negative. Rectal examination revealed a few hemorrhoids.

Stool:—Small, watery, yellow, of foul odor. Much undigested food present, mostly starch. Many red and white blood cells mixed in the small flakes of mucus. An enormous number of active trichomonads are seen.

Stomach:—Ordinary dinner removed in four hours; 150 c.c. recovered, acid and of sour odor; free hydrochloric acid, 50, total 84; no lactic acid; pepsin and rennin present. Microscopically, a few rods were seen. No trichomonads.

Blood:—Red blood cells, 4,200,000; white blood cells, 6,000; hemoglobin, 80 per cent.

Urine:—Normal in every respect.

On May 4, the patient was instructed to use a meat-free diet, and was given calomel in 1/10 grain doses, every two hours, till eight were taken. This was continued for one week, at the end of which time he was instructed to discontinue the calomel and observe the number of his daily passages. On the 12th he had three; on the 13th three; on the 14th two; on the 15th two; on the 16th three; on the 17th two. They all contained a few trichomonads, and were but partly formed. There was still some mucus, but no blood nor pus could be detected. The patient has been returned to his medication of calomel for another week and put on a more restricted diet. His blood has improved to normal, and he has regained his weight, feeling perfectly able to continue his work.

Case 10.—This patient was referred from the dermatological clinic, where he had been under treatment for urticaria, for treatment of his weakness and marked anemia. The patient is a civil war veteran, aged 62, and a farmer by occupation. He has had shortness of breath and weakness for many years, but for the past year this has been growing more pronounced. The patient gives a history of a severe diarrhea, alternating with constipation, dating from the civil war. During the war he states that he was confined to the hospital with typhoid fever, after which the diarrhea began and has given him more or less trouble ever since. At first, he would have an attack every two weeks, followed by a period of constipation. At these times he would have from 3 to 10 movements a day. The stools were of light color and contained a small amount of mucus, at times; no blood. Of late years the attacks have been growing less frequent, occurring about once a month, and lasting from 2 to 3 days. The passages are of the same character and just as numerous as before. The patient thinks that he can terminate an attack now by taking large doses of mandrake.

For the past year the patient has had some distress in his stomach after meals. He vomits occasionally, but the vomitus contained only food and mucus.

Blood examination:—Red blood cells, 4,000,000; white blood cells, 11,000: hemoglobin, 70 per cent.

Urine:—Normal.

Stool examination, after the administration of an ounce of Carlsbad salts: Large, yellow, sour, foul smelling, of amphoteric reaction. No food remains. Small amount of mucus. Many actively motile trichomonads and cercomonads seen. The former were in excess.

The patient could not stay for further treatment. He was given iron for the secondary anemia and advised to return.

In the foregoing series of cases the trichomonad is found under a variety of pathologic conditions. In some it strongly suggests itself as an etiologic factor; in others it plays a secondary part. That it is the cause of a chronic intestinal catarrh has long been held by many competent observers. Of late years, however, its influence in forms of enteritis has frequently been disputed. One reason for this has been that

we find the trichomonad living, at times, in necrotic areas, in pus and in the débris of growths. Here the trichomonad merely finds a suitable culture medium, as it is supposed to have, in the fecal material of cases of chronic diarrhea. Some observers cite instances to substantiate this view. But cases have been and are still being encountered where the intestinal conditions may be explained by the presence of these organisms. The fatal enteritis described by Galli-Valerio as occurring among guinea-pigs is proof of the fact that like parasites can cause a severe diarrhea in animals.* Furthermore, flagellate diarrhea, occurring in man, due to the *Megastoma entericum,* and infusoria diarrhea caused by the *Balantidium coli* and allied forms have been described.

There have been numerous reports in the last decade on all forms of flagellate enteritis. The work previous to that time has been classified and summed up by Janowski in an excellent manner. Notable among the series of cases that have been reviewed are those of Zunker, Grassi and Epstein. The former, in 1878, after making a systematic examination of all stools in Leyden's clinic, found nine cases of diarrhea without colic or tenesmus, in which flagellates were present. Nothnagel, soon afterward, met with the trichomonad in cases of acute and chronic catarrhal enteritis. He did not consider them harmful. Perroncito thought that a catarrh established itself through some other cause, and prepared a medium favorable for the development of the trichomonad. These organisms in their turn by irritating the epithelium assisted in maintaining the diarrhea. May, in 1892, found the trichomonad (*cercomonas coli hominis*) only in the small bowel, which was in a chronic catarrhal state. Roos made the trichomonad answerable for a persistent diarrhea. He believed that masses of them could set up a chronic irritation of the intestinal wall and cause increased peristalsis. Nothnagel's objection to this was that the bodies of these parasites were too soft to have any such effect. Grassi, though he had examined 100 cases of diarrhea in which trichomonads were found in the stool, could not make up his mind what part they played in causing such conditions. At least he did not attribute a specific action to them. Nor did von Jaksch, who found both cercomonads and trichomonads in severe enteritis of children, think they had any clinical significance.

Epstein, under the name of "Monocercomonas Diarrhea," described a severe form in 26 children. His report is an interesting as well as an important one and deserves mention in detail. There were 15 boys affected and 11 girls. He never found the condition in nursing children.

* I am aware of a similar epidemic that wiped out most of the guinea pigs in a local laboratory one spring.

The youngest was 1 year old. Seven children were between 1 and 2 years of age; 11 between 2 and 3; 2 between 3 and 4; 1 between 4 and 5, and 4 were between 5 and 6. Children older than 6 were not examined. He thought that the diarrhea caused by these organisms was the same as any other diarrhea. At times, during the first few days of the infection, a slight rise of fever occurred. Pea-soup stools were the rule; blood was rare, and the reaction was alkaline. The course was either acute or chronic. In one case that came to autopsy no organisms were found in the jejunum; a few were seen in the ileum; many were present in the ascending colon; a very great number in the transverse colon; a few in the descending colon, and none in the rectum. At one time six children were taken ill together without any notable cause. The transmission apparently took place by water and occurred mostly in the dry seasons.

Epstein cited one instance where a weak, cachectic child was fed only special liquid diet; its stools were free from parasites. Three other children who had to drink tap water suddenly developed a diarrhea with these parasites in the feces. One day the weakling was given some tap water to drink, and quickly developed the same form of enteritis. The author could not find forms in the water. He finally concluded that these intestinal conditions and these trichomonads stand in direct relation to each other. They were not found in normal stools of children, and were present only where some such digestive and intestinal disturbances were complained of.

Boas, in 1896, described some additional cases. He did not feel certain whether the trichomonads caused the diarrhea or were merely a secondary infection.

Janowski reported six cases the same year, two of which argue strongly for the pathogenicity of the trichomonad. His second patient had persistent diarrhea, with colicky pain, for some time, failed gradually and finally died. The autopsy revealed in the ascending colon small ulcers of varying size, each covered with a layer of pus and mucus. The pathologic diagnosis was chronic dysentery. His fourth case was similar. A man of 35, complaining of acute dysenteric symptoms, had from three to four daily passages, which contained pus, mucus and numberless trichomonads. His pain and diarrhea persisted for four weeks, when death occurred. His colon also contained many small ulcers running as deep as the submucosa. There was round cell infiltration about the ulcer, and many eosinophiles were seen in some areas. The fifth patient in his series developed a sudden severe diarrhea four days before admission. A great many trichomonads were found in the first stool

examined. Calomel quickly checked the rapidly-increasing diarrhea, the patient recovering in a short time.

Janowski's conclusions were finally drawn from his six observations and from a consideration of the literature. He believed that the presence of the flagellates in the intestines was in most instances without any influence on the functions of the tract. It was only rarely that they instituted either a chronic enteritis or prolonged an old condition. These conclusions seem to be at variance with his experience as well as with his comments on Case 5 and the findings and diagnosis of Cases 2 and 4. It must be agreed that these two cases are different in many respects from any other known intestinal conditions.

Skaller, in 1898, commented on flagellate diarrhea after reporting a typical case in his experience. He found the trichomonads most numerous when the stools were the most frequent. He agreed with Nothnagel that they could not cause any more irritation of the intestinal wall than masses of casein would, but thought that in many cases they were merely associated with the diarrhea. In adults no cases have been reported in which they were undoubtedly the cause of the intestinal disturbance. Strube, the same year, reported the presence of flagellates in a woman suffering from an obstinate diarrhea and secondary anemia. Cohnheim, in 1901, exhibited several cases of infusoria diarrhea, one in a woman of 24, who had suffered with "mucous colic" for two years. He found that the administration of calomel caused a disappearance of the organisms together with the diarrhea. Japha, in discussing the subject, cited the case of a child who went from clinic to clinic complaining of periodic pains in the abdomen, loss of weight, diarrhea and marked emaciation. He found trichomonads in the stools. Following the administration of large doses of quinin and tannin, the child rapidly improved. Von Leyden and Uhlmann also reported cases in this discussion, both favoring the pathogenic action of the trichomonad.

Ucke, in 1903, contributed forty cases of flagellate enteritis, most of which were due to the trichomonad. He believed that they must have some action, in that they were so frequently associated with catarrhal enteritis. The stools had one common characteristic, in that mostly all were of a thin soupy consistency and alkaline. Westphalen, in discussing Ucke's report, did not think that the trichomonad was a rare intestinal parasite. He believed, however, that the number of trichomonads was proportionate to the severity of the diarrhea.

Rosenfeld considered the possibility of them causing a diarrhea at times. He did not believe they had a toxic action, because of the absence of eosinophilia. This argument I do not think can be accepted,

for the organisms may have a local action without causing any systemic disturbances. He added that another factor could usually be found, other than the trichomonad, as the specific cause of the diarrhea, and cited several instances in proof of this assertion. In one case of *Bothriocephalus latus* and trichomonad infection, both parasites were removed. Later the patient returned with achylia gastrica. In a second case of polyposis intestinæ, with diarrhea, the trichomonads appeared late, and only at several odd times in the course of the disease.

I might mention a similar instance in the cases reported by Osborne from this clinic where four different parasites were found in the feces, but these complications are usually misleading. In Rosenfeld's second case he does not state whether the advent of the trichomonad aggravated the condition or not. From his standpoint, then, the diagnosis of a flagellate diarrhea was no cause for alarm, but rather suggested that some other etiologic factor should be sought.

Terry, in 1905, added two important cases. The first patient, a man, had suffered for over twenty-two years. At first he had slight attacks of diarrhea. Later his passages became as frequent as twelve daily, with severe griping pains in the abdomen. The trichomonads were present in large numbers. One week after admission an exploratory laparotomy was done for supposed ulcer. None was found. The patient died of general peritonitis. Autopsy revealed some small areas in the cecum, 2x4 millimeters in diameter, pale, surrounded by a darker periphera, and covered with good mucous membrane. There was a slit-like ulcer, 4 millimeters long, and extending to the muscularis. It had a necrotic floor. All the large intestine showed small erosions from the ileocecal valve on, mostly in the cecum. They had a patchy, moth-eaten appearance, and seldom involved the submucosa. The second case was in a man who had periodic attacks of diarrhea, in whose stool trichomonads were always found. The patient had a clinical diagnosis also of pernicious anemia.

Emerson, in his recent work on clinical diagnosis, is the only author up to the present time who gives more than a word of description to these flagellates. He makes this statement: " . . . We could mention one or two cases in this connection in which this parasite seems to have been the cause of a severe diarrhea." Within the last year two observations of interesting cases have been published. The first to appear, that of Biland, occurred in a boy of 17, who had suffered for many years from a diarrhea, in whose stools enormous numbers of trichomonads were seen. After a prolonged illness the patient died, and a postmortem disclosed a diffuse, small-celled infiltration of the

mucosa of the small intestine. There were places where these cells were massed, but only in the upper layers of the submucosa. In the lower part of the ileum and in the colon were small, flat ulcers penetrating to the submucosa. They had a diphtheritic surface. Many eosinophiles, mast cells and plasma cells filled the surrounding tissue. The neighboring lymphatics presented the picture of a chronic lymphadenitis. Biland fixed the stained sections of the ulcers in series, and made smears of the surface, with the hope of finding the trichomonads. Of course, he failed in this, not because of the absence of the parasites or that they were unrecognizable, but because of the impossibility of preventing plasmolysis without proper precautions in fixation and staining. Though the intestinal tract had changes seen in leukemia, pseudo-leukemia and lymphosarcoma, the author believed that these intestinal alterations were due to an action of the trichomonad, which played, therefore, an important rôle in this case of enteritis. Krause reported a case of trichomonads associated with *Balantidium giganteum* in a typhoid fever stool. His patient recovered fully. He thought that there was more against than for the opinion that the trichomonad has a specific pathogenicity.

It would seem from a survey of the reported cases of intestinal trichomonad infection that a variety of conditions are produced by this organism. Truly, it has been found associated with many pathologic states. It has been met with in children, and in some adults, in severe forms of acute, and in chronic diarrheas, where no other etiologic factor was discoverable. That such a parasite should give rise to an enteritis in some cases and not in others is possible. We know that the organism thrives best in an alkaline medium. We know that the normal gastric acidity is destructive to the parasite as well as to the cysts. Surely, then, it must be that the organism reaches the intestine at a time when the hydrochloric acid is at a minimum, a fact that holds true for many pathogenic micro-organisms. Further, the intestine may not be wholly resistant to any action on the part of the trichomonad, be this mechanical or toxic. Or the patient may have already had a chronic catarrhal condition, forming thereby a suitable medium for rapid development of these parasites. None of these facts preclude the possibility of further destructive power on the part of the parasites. So, too, it may be that in some organic condition a secondary weakness on the part of the intestinal canal opens a way for infection by the trichomonad. That we have thus far been unable to explain just how the trichomonad infects or acts does not in the least signify that it can not be the cause of an enteritis.

It has long been known that the *Amebæ dysenteriæ* produces a typical ulcer and a definite form of enteritis, acute or chronic, with periods of convalescence and with exacerbations. It has been but a short while since we have had definite ideas how it produces necrosis and sloughing. We have not been able to produce diarrhea in animals with the trichomonad as has been done in the cat with the ameba. Perhaps we have been unable to find a way of transplanting the organism so that it will resist the destructive action of the stomach. We have seen a similar form, however, one which some observers hold to be identical with the *Trichomonas hominis,* cause a fatal diarrhea in guinea-pigs with nothing more than a marked hyperemia of the intestine and an occasional ulceration. Without the evidences of infection in adults, we have the work of Epstein showing how direct infection took place in a cachectic infant and the immediate results. Why not in other susceptible individuals?

Many of the cases that have been reported present so distinct a resemblance in symptomatology and pathology to each other and to some of the cases that I have outlined, that I believe it justifiable to group these conditions and specify them under the head of trichomoniasis, which may be either acute or chronic. If Epstein's work is to be accepted, and we have no reason to doubt its accuracy, then there is surely a distinct form of flagellate diarrhea occurring in childhood.

Let us note the similarity of cases in adults. In Case 1 of my series the pathologic findings correspond very closely to those reported by Janowski in his second and fourth cases; to Terry's fourth case and to Biland's. There was no eosinophile infiltration in my case at the sides of the submucosa. It may be that the progressive pernicious anemia from which the patient suffered accounted in part for their absence. Yet the frequency of these eosinophiles in other cases tends to show that there must be some local toxic action exerted by the trichomonad.

In adults the onset of an acute case is usually accompanied by severe abdominal pain, often colicky in character, radiating from side to side, and more or less constant. Nothing relieves it when at its height, except opiates. The stools are not necessarily frequent in these cases, but are usually increased in number, unformed or of fluid consistency. In Case 7, however, the patient never noticed any difference in their appearance, except after the use of cathartics. They are invariably alkaline and usually of a yellowish brown color. The trichomonads are present in enormous numbers, especially at the height of an attack, as, for instance, in Case 5, where I counted an average of eighty-two in a field, with a one-seventh Leitz objective No. 2 eyepiece. When convalescence sets in their number diminishes.

It might be argued that in each of my cases trichomonads were not found immediately after the onset of the symptoms. In chronic cases, however, each exacerbation was accompanied by an increase in the trichomonads in the stools. One interesting feature, and in this respect it resembles Terry's second case, is the fact that Cases 1 and 6 were clinically cases of pernicious anemia. Whether the diarrhea, which is a common symptom of pernicious anemia, existed previous to the trichomonad infection, or the flagellates caused the enteritis, which, followed by a secondary anemia, gradually developed into the pernicious type, would be difficult to determine.

Some writers claim to have found the trichomonad in normal feces. In Case 7 they existed in a stool of normal consistency, but there were symptoms in this instance undoubtedly due to the presence of these parasites. I have examined for them for four months at different seasons of the year in stools of patients that were given an ounce of Carlsbad salts on admission, and have never found them, except in cases where intestinal complaints were manifested. Furthermore, they have not been found in the routine examinations carried on in the medical clinic in other intestinal cases.

There is no doubt about the efficacy of calomel in destroying the trichomonad. In fact, it is usually found that after the administration of small, repeated doses, the diarrhea diminishes, the pain ceases and the patient rapidly recovers. Other drugs, such as quinin, tannin, salol, thymol, naphtholen and beta-naphthol, have been employed at times with some success.

With our limited knowledge of the reproduction and cultural characteristics of the trichomonad the method of entrance into the intestinal tract can not readily be determined. The most likely way is through food and drink, whereby the spores are ingested. The small intestine is frequently the seat of these organisms, as can be shown by irrigating the colon and giving a saline cathartic; then examining the feces for active forms, before and after, in both instances. The commonest seat is the large intestine from the cecum to the sigmoid colon. It is in the ascending and the transverse portions of the colon that the ulcers are usually met with and most of the round cell infiltration occurs.

It is not my intention to speculate on the manner in which the trichomonad brings about these intestinal changes. The mechanical theory is not a likely one. That the trichomonad produces a toxin is plausible. To presume that this toxin is a secretion, or the result of the activity of the organisms on the intestinal contents, would not be justified. Withal, I firmly believe that the trichomonad is the direct cause of certain forms

of acute, chronic and recurring enteritis, characterized by abdominal pain, diarrhea, loss of weight and strength, with slight temperature at times, and anemia. Whatever may be the immediate result of its introduction into the intestinal tract, this fact remains, that its removal or a great reduction in the number of organisms present usually results in a marked lessening of symptoms or a complete recovery.

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AN EXPERIMENTAL STUDY OF THE ACTION OF OIL ON GASTRIC ACIDITY AND MOTILITY.

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This investigation was commenced with the idea of perfecting a method of experimentation on the human stomach which has been employed more or less systematically in the medical clinic of the University Hospital for a number of years.[1] Much of the knowledge concerning the action of the various drugs and remedies administered in the treatment of stomach disorders has been deduced from the results of purely empirical procedures. In recent years, however, quite a number of scientific experiments have been conducted, particularly in Europe, which furnish the profession much useful information concerning food reactions in the stomach. Some of the methods employed to solve certain problems regarding digestion are fairly accurate, while others are subject to more or less criticism; consequently the chief aim of this study has been to overcome these defects in so far as possible. Notwithstanding the difficulties of this task, it seemed possible that by paralleling Pawlow's classic experiments on dogs one might obtain evidence justifying the conclusion that all reactions obtained by experimentation on canines with miniature stomachs occur to a greater or less extent in man.

The authors had been employing olive oil as a routine treatment for hyperchlorhydria in all its forms, both in hospital and private practice, for a number of years, with such favorable results that the desirability of determining its effects on the gastric functions experimentally prompted the present investigation herewith reported. Results of clinical observations, which are not based on technical experimentation, have revealed many indisputable truths concerning digestion, but the science of medicine will be advanced greatly if these observations can be confirmed and the action of drugs demonstrated by actual experiment.

It is an ancient idea that fats retard digestion. Aristotle evidently observed phenomena of this nature before expressing the opinion: "Now the best digestion is in the bottom of the stomach, because the fat

1. Cowie: Physician and Surgeon, Detroit and Ann Arbor, 1903, xxv, 241-252.

descends not there; such as eat fat meat are very sleepy, by reason that digestion is hindered." Pawlow[2] has aptly said that "physiology stood for a long time in sharp conflict with practical medicine. Physicians bringing forward their observations in proof had long answered the question in the affirmative. . . .

"Physiologists, on the other hand, had fruitlessly endeavored, for decades, to arrive at definite results." Dr. Chigin,[2] working in Pawlow's laboratory, demonstrated that fat and starch have no exciting effect on the glands of the dog's stomach. Pawlow devoted particular attention to the investigation of vegetable and animal fats. "They were tested not alone on a dog with an isolated miniature stomach, but also on animals with gastric and esophageal fistulæ, and finally on dogs which had survived the operation of separation of the vagi in the neck, performed several months previously." In all cases the fat was directly introduced into the stomach without swallowing. The results were negative.

When this experimenter poured 100 c.c. of oil into the main stomach of a dog by means of a "sound," and one-half to one hour later the dog was given 400 grams of flesh, instead of the usual five to ten minutes, half an hour elapsed before the beginning of secretion, and when it commenced it was scanty, only three to five c.c. being collected in from two to three hours, while under other conditions ten to fifteen c.c. were secreted in the same time. When the oil was introduced into the stomach immediately after eating the meat, "the secretion began with normal energy, and only later did the inhibitory influence make its appearance." "The same results were obtained when the dog was given fat mixed with meat." A lowering of the digestive function as well as the amount of juice was noticed.

Pawlow concludes that "fat depresses, that is, inhibits the normal energy of the secretory process," and is forced to the further conclusion that this inhibition is central, by reflex stimulation of the inhibitory nerves of the glands, or the inhibitory centers of these nerves, and not to the mere mechanical effect of covering over the mucous membrane and preventing excitation of the nerve endings.

Backman,[3] in his investigation, first washed the fasting stomach with warm water, after which he administered daily alternations of fat and fat-free food. Samples were obtained by expression, at intervals of one-quarter to one-half hour, until the stomach was empty, which was proved subsequently by washing. Similar investigations with and with-

2. Pawlow: The Work of the Digestive Glands, lecture, translated by W. H. Thompson, London, 1903, 80.

3. Backman: Ztschr. f. klin. Med., 1900, xl, 224.

out the fat were usually conducted two or three times with the same meal. Unfiltered contents were used for the determination of the acids. The meals employed were the following:

I. French bread ..... 100 grams.
Butter ..... 50 grams.
Water ..... 300 grams.
II. French bread ..... 100 grams.
Cream ..... 300 grams.
III. Oatmeal porridge, made of 6 grams of oatmeal, steamed with enough water to make 357 grams. To this 50 to 199 grams of butter were added during the cooking.

From his investigations Backman concluded that HCl was decreased from 2 to 42 per cent. by the employment of fat, these figures being obtained with the cream meal. He also found that butter delayed the appearance of free HCl in one of his cases, and that cream delayed it in two cases out of three. The rise of the acidity curve, which is slower with fat than without, often lasts until the end of digestion, exhibiting marked contrast with the control meals, in which the highest values for free HCl are in the middle of the digestion period. In other words, there is a decline in the secretion of the gastric juice and a lengthening of the time of digestion when oil or fat is ingested with the meal.

Strauss and Aldor[4] report experiments on seven cases of hyperchlorhydria. Their purpose was to determine the effects of the substitution for carbohydrates of fat given in abundance, but in quantities not so large as to cause discomfort of the patient or to interfere with the assimilation of fat. They employed three sets of meals:

I. Control meal, consisting of one roll and 300 c.c. of tea. This was allowed to remain in the stomach one hour.
II. Gum arabic meal, consisting of one roll, 300 c.c. of tea, and 5 grams of gum arabic.
III. Oil meal, consisting of one roll, 300 c.c. of tea, 5 grams of gum arabic, and 30 grams of oil of sweet almonds.
IV. Olive oil meal, consisting of one roll, 300 c.c. of tea, 5 grams of gum arabic, and 60 grams of olive oil.

Seven cases in all are reported. All the cases, except 2 and 5, received two control meals. Cases 3 and 4 received one initial meal and one gum meal as control. In five of the cases there was a diminution in the values of the acids as contrasted with the controls. This was marked in Cases 1, 3 and 4. Cases 2, 3, 4 and 7 show variations which are certainly not marked, except in Case 3, where, after the gum meal, the HCl value rose from 8, with the previous meal, to 35, and fell to 10 and 6

4. Strauss and Aldor: Ztschr. f. Diätet. u. physik. Therap., Leipz., 1898. i. 117.

with the oil of sweet almond meal. The increase from 8 to 35, the authors assert, is due to the action of the gum arabic, which had a similar action in nearly all of the cases. So far as this part of their work is concerned, Strauss and Aldor reach the conclusion that oil depresses the secretion of acid. It would seem that their cases were not sufficiently controlled nor sufficient in number to justify very definite conclusions.

Ewald and Boas[5] employed a test meal consisting of 1 to 2 per cent. starch paste and pure neutral olive oil in the proportion of four to one. They conclude that after the administration of a mixture of paste and oil, as contrasted with paste alone, no free HCl appears during the first half-hour.

Akimow-Peretz[6] investigated the effect of the daily administration of almond oil over long periods. Fifty to 100 c.c. were given before eating. A lowering of the acidities in 16 out of 18 cases was found. An emulsion of almonds made by grinding up a tablespoonful of sweet almonds into a meal, and adding boiled water, so that the amount of the strained fluid, after thoroughly shaking, equaled about 300 c.c., gave similar, but not so marked, results.

ORDER OF AUTHORS' INVESTIGATION.

1. The patient was chosen with much care. He was one who had first become thoroughly familiar with the manipulations of the stomach tube, that is, he could swallow it without discomfort or retching, was able to retain it for an indefinite period of time, and to prevent the saliva from entering the stomach in any undue amount. The cases studied at the University Hospital were admitted for stomach complaints. Those patients examined at the Craig Colony presumably had normal stomachs; at least none of them complained of gastric symptoms.

2. A uniform test meal was employed in each case so that the food stimulation would not vary from day to day. It was given at approximately the same time each day and was removed from the stomach at a definite time after eating. The patients studied at the University Hospital were given a shredded wheat biscuit, which has a fairly constant weight of 30 grams, and, after eating this dry, 300 c.c. of water. At the Craig Colony, 30 grams of very dry toast, with at first 400 c.c. and later 300 c.c. of water, were given. Olive oil was used almost exclusively at the University Hospital. Cotton seed oil was given preference at the Craig Colony, olive oil being used only a few times.

3. After the secretion range was established by a series of meals the

5. Ewald and Boas: Arch. f. path. Anat. (etc.), Berl., 1886, civ, 271.
6. Akimow-Peretz: Abstract, Arch. f. Verdauungskr., Berl., 1898, iv, 397.

oil was given at a definite time in relation to the meal and the examinations conducted in the same way as with the controls until a sufficient number were obtained. If the patients remained in hospital long enough, the oil was withdrawn and the tests continued.

4. Two series of experiments were conducted in every case, one as described above, where the contents were recovered one hour after ingestion, and the other by what is designated the special meal series, in which samples were removed from the stomach at frequent intervals, 5, 10 or 15 minutes, until the stomach was empty. A final lavage was given to assure the removal of all food from the stomach; a definite amount of water was employed. The reactions of the fluid obtained after the lavage were also tested. In the beginning of the investigation, the tube was allowed to remain in the stomach during the entire stage of digestion. Later the tube was removed after each sample was obtained.

5. The chemical analyses consisted in the estimation of free HCl with di-methyl-amido-azo benzol as indicator; of the total acidity with phenolphthalein as indicator; of peptic strength by Mett's method.[7] To eliminate the personal equation, each case was studied by the same person. This rule was rarely broken. However, we had determined by testing ourselves that we read to the same end reaction.

By adhering as closely as possible to these procedures and by examining a sufficient number of cases, we have hoped to eliminate many factors of error which must necessarily exist in an investigation of this nature.

The effect of oil was investigated on three definite functions of the stomach—on the rate and height of secretion and on the drainage or motor power of the stomach. Final conclusions concerning each of these are based on comparisons of the average results of large numbers of meals with and without oil administered in definite relation to the meal.

ILLUSTRATIONS OF THE IMPORTANCE OF CARE IN THE SELECTION OF SUITABLE CASES FOR EXPERIMENTATION.

The following cases are only a few of the many that can be given from the clinical records of the University Hospital illustrative of how useless any investigation would be without first having controlled the range of secretion by keeping the subject under the same conditions from day to day. It was pointed out many years ago by Ewald, in the first edition of his Klinik der Verdauungskrankheiten (1888), that there is often a daily difference of from 20 to 27 degrees of acidity in

7. Cowie: Physician and Surgeon, Detroit and Ann Arbor, 1904, xxvi, 118-121.

the normal stomach. From a perusal of the literature it would seem that this fact had not been much considered.

CASE 1.—Louis M.

	Free HCl.	Total acid.
Dec. 16, 1904	26	42
Dec. 17	0	16
Dec. 18	0	12
Dec. 19	10	28
Dec. 20	22	40
Dec. 21	30	46
Dec. 22	34	52

Stimulus equivalent to an Ewald test breakfast.

CASE 2.—Miss A. K.

	Free HCl.	Total acid.
Feb. 23, 1905	28	28
Feb. 24	40	48
Feb. 25	48	60

CASE 3.—Mr. B.

	Free HCl.	Total acid.
Oct. 4, 1904	0	4
Oct. 5	0	15
Oct. 7	0	15
Oct. 8	0	12
Oct. 26	0	10
Oct. 27	0	20
Oct. 28	10	35
Nov. 7	0	50
Nov. 15	10	30
Nov. 16	8	26
Feb. 22, 1905	0	30
Feb. 24	0	28
Feb. 25	0	14

CASE 4.—A young man with hyperacidity. The fasting stomach showed, on March 24, the presence of HCl and pepsin. After a shredded wheat biscuit meal, samples were taken every fifteen minutes. The first apearance of HCl (Günzburg) was noted at 52 minutes. The highest HCl value, 42, was obtained at 67 minutes. The stomach was empty at 112 minutes, and the total amount recovered during this time was 151 c.c. The following day, March 25, the fasting stomach was empty. Two ounces of cotton seed oil were given one-half hour preceding the shredded wheat biscuit meal. The first appearance of free HCl was at 69 minutes. The highest free HCl value, 31, was obtained at 129 minutes. The stomach was empty at 159 minutes, and the total amount recovered during this time was 218 c.c. April 1, two ounces of cotton seed oil were given, as before. There was no HCl secreted during the hour. April 2, no oil preceded the biscuit meal, and no HCl was secreted.

In Cases 1 and 3 one could easily choose three successive meals which might suggest a condition directly opposite to that which was dominant. Case 4 shows how incomplete work might have given an apparent basis for very definite conclusions as to the action of olive oil. Had the fourth meal not been given, the conclusion might have been reached that an excellent demonstration of the depressant action of oil on the acidity had been obtained. The fourth meal, however, obviates any such conclusion and shows that the secretion in this case was disturbed by nervous influences.

SERIES 1.—The following are the cases studied at the University Hospital:

CASE 5.—Mr. F. This patient had a distinct chemical hyperchlorhydria without subjective symptoms, excepting constipation. He had attacks of nocturnal unconsciousness, accompanied by vomiting and frothing at the mouth, followed by pain in the stomach and soreness of the abdominal muscles. No attacks during investigation.

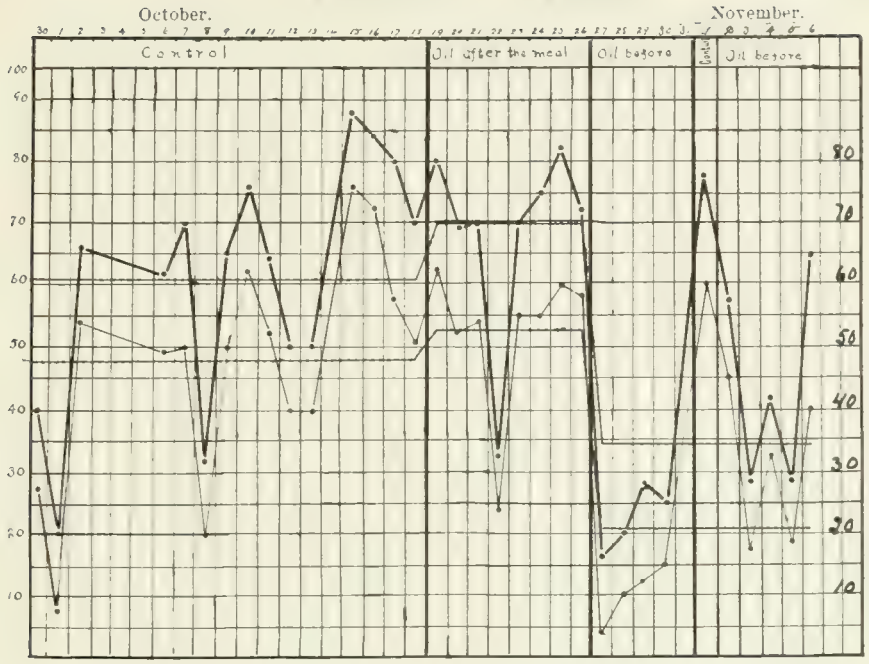

Chart 1, Case 5.—Mr. F. Record of daily meals. Total acid indicated by upper (heavier) solid line. Free acid indicated by lower solid line. Average total acidity indicated by upper dotted line. Average HCl indicated by lower dotted line.

EXPERIMENT 1.

Date.	Quantity.	Free HCl.	Total acid.	
Sept. 30	30 c.c.	27 c.c.	40 c.c.	Control.
Oct. 1	35	7	19	Control.
Oct. 2	160	54	66	Control.
Oct. 6	120	49	63	Control.
Oct. 7	15	50	70	Control.
Oct. 8	10	20	32	Control.
Oct. 9	10	50	65	Control.
Oct. 10	40	62	76	Control.
Oct. 11	40	52	64	Control.
Oct. 12	7	40	50	Control.
Oct. 13	..	40	50	Control.
Oct. 14	0	..	..	Control.
Oct. 15	75	76	88	Control.
Oct. 16	75	72	84	Control.
Oct. 17	25	57	80	Control.
Oct. 18	..	51	70	Control.
Oct. 19	75	62	80	Oil, 1 oz. after.
Oct. 20	50	52	69	Oil, 1 oz. after.
Oct. 21	30	54	70	Oil, 1 oz. after.
Oct. 22	172	24	34	Oil, 1 oz. after.
Oct. 23	48	55	70	Oil, 1 oz. after.
Oct. 24	40	55	75	Oil, 1 oz. after.
Oct. 25	110	60	82	Oil, 1 oz. after.
Oct. 26	75	58	72	Oil, 1 oz. after.

Date.	Quantity.	Free HCl.	Total acid.	
Oct. 27	175	4	16	Oil before.
Oct. 28	180	10	20	Oil before.
Oct. 29	208	12	28	Oil before.
Oct. 30	..	15	25	Oil before.
Oct. 31	5	0	10	Fasting stomach.
Nov. 1	150	60	78	Oil after.
Nov. 2	115	45	57	Oil before.
Nov. 3	254	17	28	Oil before.
Nov. 4	210	32	42	Oil before.
Nov. 5	228	18	28	Oil before.
Nov. 6	60	40	65	Oil before.
Nov. 7	Special meal.			
Nov. 8	Special meal.			
Nov. 9	Special meal.			

EXPERIMENT 2.

CASE 5.—Mr. F. Control meal. XI-9-1903.

Time.	Amount.	Free HCl.	Total acid.	Pepsin.	Pepsinogen.
6:35	Began eating.				
6:42	Finished eating.				
6:45	10 c.c.	0 c.c.	0 c.c.	0 c.c.	3.61 c.c.
6:50	11	0	0	0	6.7
6:55	9.5	4	10	0.36	13.6
7:00	12	10	21	2.56	
7:05	11	19	32	4	
7:10	10	21	40	9	
7:15	10.5	20	40		
7:20	10	25	50	6.7	
7:25	10	30	56	9	
7:30	11	40	60	12.2	
7:35	10	40	62	10.9	
7:40	9.5	48	68	15.2	
7:46	10	40	68	16	
7:50	10	30	52	11.2	
7:55	5	28	50	9.61	
8:00	Lavage.	Practically clear.		Free HCl, 11 c.c.	

Meal with oil immediately before eating. XI-7-1903.

8:10	Began eating.				
8:17	Finished eating.				
8:20	10 c.c.	0 c.c.	0 c.c.		2.89 c.c.
8:25	11	0	7		2.56
8:30	10	0	0		1.4
8:35	13	0	7.5		2.56
8:40	11	10	20		3.24
8:45	10	10	20		4
8:50	10	0	10		...
8:55	11.5	18	30		3.24
9:00	8	16	28		4.41
9:05	11.5	16	30	1.96	
9:10	10.5	20	29		
9:15	10	19	28	6.76	
9:20	10	40	57	9	
9:25	10	40	50	10.9	
9:30	10	30	46	9	
9:35	10	32	42	4	
9:40	5	33	45	9	

Lavage clean. Free HCl, 10 c.c.

In Charts 2, 3, 7, 8, 9, 10 and 11 the figures at the top in minutes represent the time subsequent to the beginning of eating.

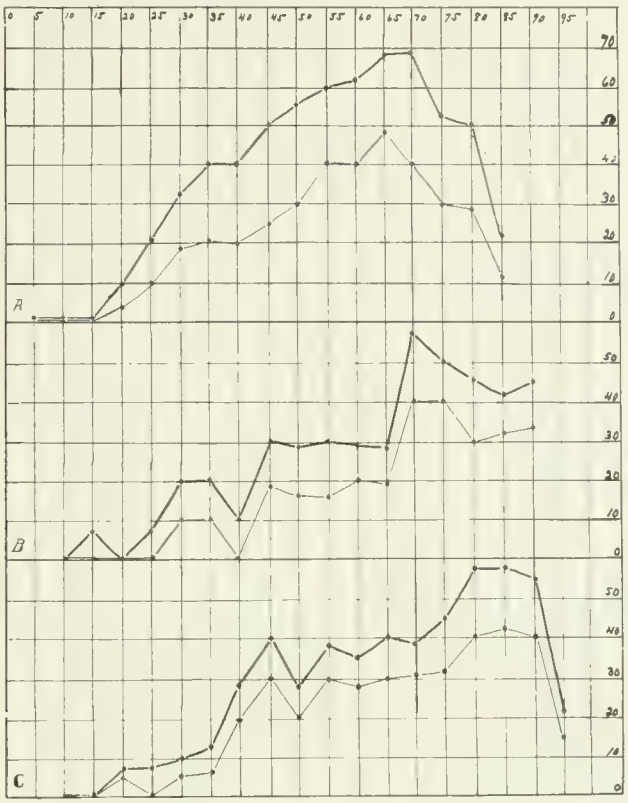

Chart 2, Case 5.—A, control. B, olive oil immediately preceding the meal. C, olive oil immediately after the meal.

Case 5.—Mr. F. Oil immediately after meal. XI-8-1903.

Time.	Amount.	Free HCl.	Total acid.	Pepsin.	Pepsinogen.
8:15	Began eating.				
8:23	Finished eating.				
8:25	10 c.c.	0 c.c.	0 c.c.	.	15.3 c.c.
8:30	10.5	0	0	. .	12.9
8:35	10	5	7	. .	14.4
8:40	10	0	7	. .	8.4
8:45	10	5	10	0	
8:50	10	26	13	. .	
8:55	10	20	28	10.5	
9:00	10	30	40	24	
9:05	10	20	28	13.4	
9:10	10	30	38	18.5	
9:15	10	28	35	27	
9:20	10	30	40	22	
9:25	11	31	38	18.5	

Time.	Quantity.	Free HCl.	Total acid.	Pepsin.	Pepsinogen.
9:30	10	32	46	19.4	
9:35	10	40	57	18.5	
9:40	10	43	57	20	
9:45	8	40	55	23	
9:50	*Lavage about clean. HCl, 15 c.c.				

*Order of investigation.

From a study of these tables and the accompanying charts the following deductions can be made:

1. In the daily meals, Table 1, the oil was given in close relation to the meal. When it was given immediately after the meal, there was practically no change in the acid values over those of the control meals, but the progress of digestion was somewhat delayed. When the oil immediately preceded the meal, a decided decrease in the amount of the free acid was noticed. On November 1 a mistake was made and the oil given immediately after the meal, and the same result was obtained as in the previous administration of oil at this time. However, on November 2 and 6 a somewhat similar comparative lack of depression occurred when oil was administered before the meal.

2. The special meals show that the appearance of free HCl is distinctly delayed when oil is given before the meal, but is unaffected when oil is given after the meal. The height of secretion is greatest when oil is not used; it is apparently slightly lowered when oil is given either before or after the meal, and is distinctly delayed when oil is given after the meal.

3. The rate of increase in the quantity of free HCl is delayed by oil before or after the meal; this delay is more marked when oil is given before the meal. The curve of the rise of the acidity may be said to be concave with oil and convex without oil. Taking the readings one hour after each of the special meals, the free HCl is distinctly lower where oil was administered before the meal than after meals without oil; when oil was given after the meal it is only slightly lower, corresponding closely with the results obtained in the daily meals. The case did not remain long enough to enable any conclusions as to the permanency of the effect of the oil treatment. This will be discussed later.

4. Variations in the amount of HCl observed may be due not to the lessened secretion, but to the retarded secretion. In the special meals the secretion often rises as high, but the rise is markedly delayed by the oil, and at the end of the usual time at which a test meal is removed from the stomach the acid value is distinctly lowered.

Case 6.—Mr. J. Peptic ulcer; subacute; hypersecretion; robust railroad conductor; symptoms of hyperchlorhydria marked. Operation, gastroenterostomy; recently active ulcer; recovery complete.

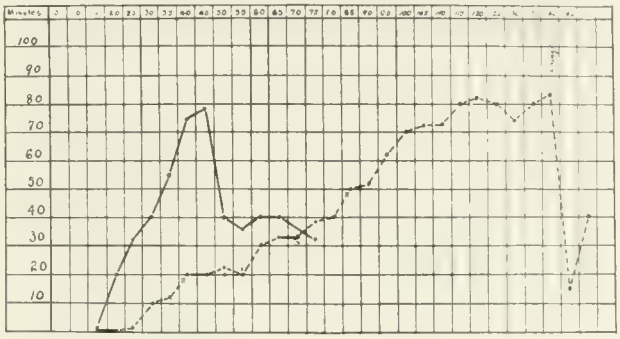

Chart 3, Case 6.—Mr. J. Experiment 1, control meal indicated by solid line. Olive oil meal indicated by dotted line.

EXPERIMENT 1A.—MR. J., SHREDDED WHEAT BISCUIT MEAL WITHOUT OIL.

Time.	Quantity.	Free HCl.	Total acid.	Peptic value.	Lugol reaction.	Remarks.
7:55 a. m.	After lavage began eating.					
8:00	Finished eating.					
8:03	11 c.c.	03 c.c.	12 c.c.	0.00 c.c.	B V	
8:08	10	20	30	10.24	V B	
8:13	10	33	49	20.25	V B	
8:18	10.5	40	53	16.00	V B	
8:23	10	55	70	12.25	V B	
8:30	10.5	75	90	14.44	V B	
8:31	8.5	78	98	6.25	V B	
8:47	11	40	52	7.84	A C	Viscid.
9:03	11	37	50	6.76	A C	More viscid.
9:18	11	40	57	23.04	A C	Very viscid.
9:28	10.5	40	60	9.00	A C	Less viscid.
9:30	5	..	..	.....	...	
9:40	9	32	42	14.44	A C	
9:48	Stomach washed. No HCl in washings.					
9:53	Tube passed, aspiration continued for three minutes., 1 c.c. viscid fluid. No reaction for HCl.					

Case 6.—Mr. J.

EXPERIMENT 1B.—MR. J., SHREDDED WHEAT BISCUIT MEAL PRECEDED BY OIL.

Time.	Quantity.	Free HCl.	Total acid.	Peptic value.	Lugol reaction.
8:10½	After lavage 50 c.c. of olive oil was taken.				
8:12¼	Began eating the test meal.				
8:20	Finished eating.				
8:26	10.5 c.c.	0 c.c.	? c.c.	0	B
8:31	11.0	0	10	0	V B
8:36	12.75	..	15	0	V B
8:41	10.0	10	20	0	V B
8:46	10.0	12	22	2.25	V B
8:51	10.0	20	30	2.89	V B
8:56	10.0	20	30	6.25	B V

Time.	Quantity.	Free HCl.	Total acid.	Peptic value.	Lugol reaction.
9:01	10.0	22	33	6.25	B V
9:06	10.0	20	30	10.8	B V
9:11	10.0	30	40	5.29	B V
9:16	10.0	33	45	7.84	B V
9:21	11.0	33	44	5.29	V B
9:26	10.0	38	48	7.84	B V
9:31	10.0	40	55	10.8	V B
9:36	10.0	50	62	10.8	B V
9:41	11.0	53	70	16.8	B V
9:46	11.0	62	78	7.84	BB V
9:51	10.0	70	85	7.29	B V
9:56	10.0	73	90	10.8	VV B
10:01	10.0	73	88	10.8	VV B
10:06	10.0	80	92	12.25	VVV B
10:11	10.0	82	96	10.08	VVV B
10:16	10.0	80	100	7.29	VV B
10:21	10.0	76	90	18.49	B
10:26	10.0	80	95	22.09	A C
10:31	20.0	83	100	28.09	A C
10:31	Stomach washed. water returns clear dimethyl-amidoazobenzole.				
10:36	11 *	15	30	10.8	B V
10:41.....	5.5	40	50	8.6	B V

Lavage after last sample contained no free HCl.

Few flecks of meal.

CASE 6.—Mr. J.

EXPERIMENT 2.—ORDINARY DAILY SHREDDED WHEAT BISCUIT MEALS, OIL AS SPECIFIED.

Date.	Quantity.	Free HCl.	Total acid.	
April 9	76 c.c.	62 c.c.	72 c.c.	Control.
April 10	120	78	88	Control.
April 11.....	120	66	74	Control.
April 12	120	70	88	Control.
April 13	75	52	60	Control.
April 14	65	50	59	Control.
April 15	60	52	62	Control.
April 16	55	88	81	Control.
April 17	280	22	34	Oil before.
April 18	130	38.6	54	Oil before.
April 19	173	10	26	Oil before.
April 20	195	44	60	Oil before.
April 21	220	14	30	Oil before.
Average	74	62.5	73	8 without.
Average.....	199.6	25.7	41	5 with.

In this case a most pronounced change is seen in the rate and height of secretion, as well as in the motor power. With the special meal there is a distinct lengthening of the digestive period. Digestion, instead of continuing one hour and forty minutes, as it did in the control meal, was lengthened to two hours and ten minutes when the meal was preceded half an hour by oil. In the oil meal the rate of secretion of hydrochloric acid was markedly retarded. With the control meal a free acid value of three was obtained 12 minutes after beginning to eat; with the

oil meal 23½ minutes elapsed before the faintest reaction for free acid could be demonstrated.

The height of digestion, 78, with the control meal was reached in the middle of the digestive period, 40 minutes after beginning to eat, while with the oil meal the height, 82 to 83, was attained at the end of the

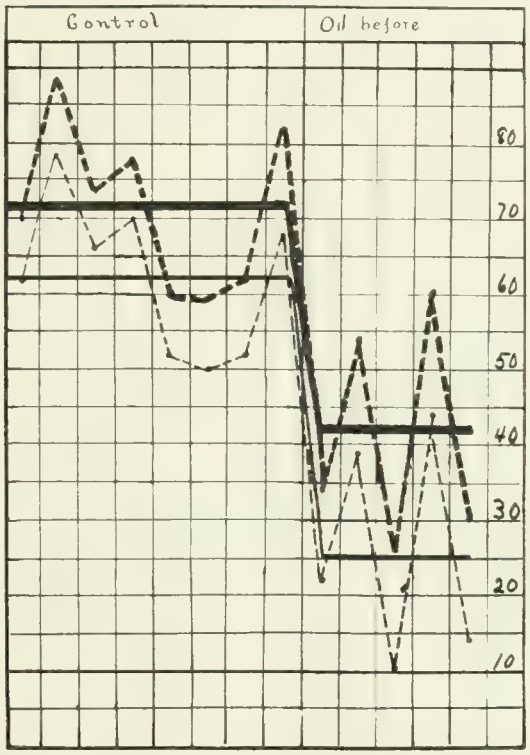

Chart 4, Case 6.—Mr. J. Daily meals. The upper and heavier dashed line is the total acidity curve, which is averaged in the solid, heavier line; similarly, the HCl is shown in the lower dashed line and this is reduced to average in the lower solid line.

digestive period, about two hours after beginning to eat. The total output of HCl has, by this time, reached a quantity considerably above that observed in the control meal.

The motor power is distinctly lowered by the oil. With the control 128 c.c. were recovered during the stage of digestion; with the oil meal over twice as much, 277 c.c., were obtained. At the end of one hour, the usual time a test breakfast is permitted to remain in the stomach, the

secretion with the control meal is slightly in advance of that in the oil meal.

With the peptic values there is a change corresponding in each meal with the change in the acids.

Doubtless little reliance can be placed on Lugol's test for starch digestion in an experiment of this character. It would be reasonable to expect that, with 23 minutes of practically achlorhydria, much, if not nearly all, of the starch would have undergone the change to anachrom. With the oil meal anachrom was not obtained until the end of digestion, when the free acid was excessively high. The erythrodextrin stage was quickly reached in each case. For this reason the tests were not continued in the other cases.

The daily meals show similar effects from the oil. The height of the secretion is, however, more markedly lowered with the oil meals. The decrease in motor power in the oil meals is as striking as it is in the special meal, the average amount recovered being nearly three times as much as the control. This rather tends to strengthen the value of the special meal, which, together with the daily meals, may be said to be fairly representative of what actually takes place in this case after oil is administered.

CASE 7.—Mr. N. Stomach neurosis.

Date.	Amount.	Free HCl.	Total acid.	Peptic value.	Remarks.
October 27, 1903...	100 c.c.	32 c.c.	70 c.c.	4.84	Control meal.
October 28.....	74	55	75	4.41	Control meal.
October 29.....	75	52	66	12.25	Control meal.
October 30.....	96	50	64	16.00	Control meal.
October 31.....	74	49	64	5.29	Control meal.
November 1.....	..	52	64	4.84	Control meal.
November 2.....	25	45	60	10.24	Control meal.
November 3.....	60	52	67	4.90	Control meal.
November 4.....	80	54	66	4.41	Control meal.
November 5.....	90	26	42	1.60	Oil given ½ hr. before.
November 6.....	50	50	62	5.10	Oil given ½ hr. before.
November 7.....	300	0	11	0.00	Oil given ½ hr. before.
November 8.....	199	58	78	2.60	Oil given ½ hr. before.
November 9.....	120	56	70	20.50	Oil given ½ hr. before.
November 10.....	65	39	59	3.01	Oil given ½ hr. before.
November 11.....	70	60	75	16.00	Oil given ½ hr. before.
November 12.....	92	66	80	21.78	Oil given ½ hr. before.
November 13.....	102	32	42	3.02	Oil given ½ hr. before.
November 14.....	70	52	66	9.93	Oil given ½ hr. before.
November 15.....	62	38	57	9.27	Oil given ½ hr. before.
November 16.....	70	54	69	1.06	Oil given ½ hr. before.
November 17.....	152	0	13	0.00	Oil given ½ hr. before.
November 19.....	71	60	70	.....	Oil given ½ hr. before.
November 20.....	118	8	22	0.28	Oil given ½ hr. before.
November 21.....	68	48	64	14.06	Oil given ½ hr. before.

In this case no special meals were given. The acidity curve for the nine days preceding the oil meals was comparatively constant. The fluctuations were within fairly narrow limits. As soon as the oil is given, wide variations are noted. At one time, November 7, there was no secretion of free acid, and the total acidity was only 11; the motility was also markedly lowered, 300 c.c. being recovered at the end of one hour. After this the fluctuations continued within wide limits, touching zero again in ten days, but with a less marked lowering of the motility. On the twentieth day the HCl dropped to 8, but the same stimulus gave an acidity of 48 on the following day.

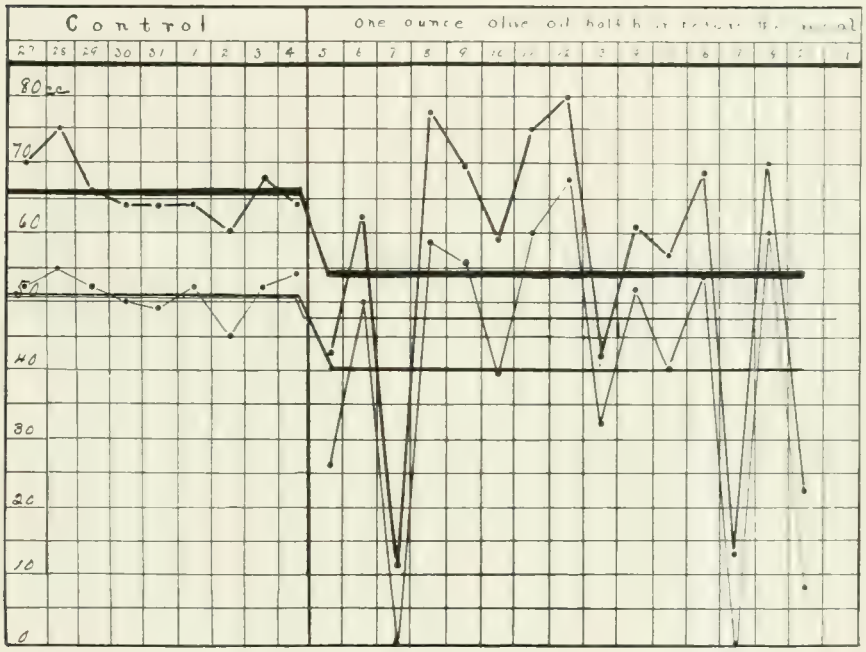

Chart 5, Case 7.—Daily meals. The upper broken line is the total acidity curve, which is averaged in the upper continuous line. The HCl is shown in the lower broken line, and reduced to average in the lower continuous line.

If a curve of the average for the control and the oil meals be plotted, a distinct depressant effect from the oil is noted. In the presence of two 0 and one 8 acid values that can not be explained, it is a question whether the average lines should be so low. Omitting the records of November 7, 17 and 20, the average line comes to 40.8. That there is depression from oil on the 5th, 10th, 13th and 15th is unquestioned. On the other days nervous factors may have been at work with which we could not acquaint

ourselves in the period of nine days which seemed long enough for a control. The great variation in the acidity after the beginning of the administration of oil suggested that it would be of interest to continue the observations, but the patient had to leave before a second series of controls could be carried out. Such controls seem very important in order to allow a proper interpretation of this case. There can be no question but that oil has at various times had a decided depressant effect both on the secretions and the motility.

Chart 6, Case 8.—A. P. J. Daily shredded wheat biscuit meals. Upper solid line indicates total acid. Dashed line indicates free acid. Lower and heavy solid line indicates average free acid.

CASE 8.—Mr. A. P. J. Hyperchlorhydria with symptoms. No ulcer.

DAILY MEALS WITH AND WITHOUT OLIVE OIL.

Date.	Amount.	Free HCl.	Total acid.	Peptic value.	Remarks.
November 17, 1903.	40 c.c.	94 c.c.	114 c.c.	1.0	No olive oil.
November 18.....	100	90	106		No olive oil
November 19	100	88	104	5.24	No olive oil.
November 20.....	85	94	112	4.4	No olive oil.
November 21.....	82	93	111	4.4	No olive oil.
November 22.....	80	92	102	5.6	No olive oil.

Date.	Amount.	Free HCl.	Total acid.	Peptic value.	Remarks.
November 23	60	96	106		No olive oil.
November 24	100	96	112		1 oz. immediately before.
November 25	100	80	100		1 oz. immediately before.
November 26	100	80	96		1 oz. immediately before.
November 27	90	84	96		1 oz. immediately before.
November 28	110	84	100		1 oz. immediately before.
November 29	125	84	108		1 oz. immediately before.
November 30	130	60	86		2 oz. immediately before.
December 1	95	70	92		2 oz. immediately before.
December 2	105	68	87		2 oz. immediately before.
December 3	110	86	102		2 oz. immediately before.
December 4	110	58	78		2 oz. ½ hr. before.
December 5	130	42	54		2 oz. ½ hr. before.
December 6	125	64	84		2 oz. ½ hr. before.
December 7	80	48	64		2 oz. ½ hr. before.
December 8	95	64	88		2 oz. 10 min. before.
December 9	100	54	72		2 oz. 10 min. before.
December 10	110	48	60		2 oz. 10 min. before.
December 11	95	60	78		2 oz. 10 min. before.
December 12	105	64	82		2 oz. 10 min. before.
December 13	60	66	76		No oil before.
December 14	95	108	118		No oil before.
December 15	95	94	108	4.00	No oil before.
December 16	110	96	106	6.25	No oil before.
December 17	90	84	96	5.03	No oil before.

This case was observed for thirty days. The first control series consisted of seven meals. The second control series, beginning on the twenty-sixth day, consisted of five meals, making twelve control meals in all. The effect of dosage, as well as time of administration, of the oil is well illustrated in the average free hydrochloric acid curve. Two ounces of oil immediately preceding the meal causes a decidedly greater depression than one ounce. Two ounces half an hour before the meal brings about a still more marked depression of the secretions. It would seem that in the second instance the increase in the amount of oil accomplished exactly what increase in time before the meal did in the third instance. Two ounces of oil should spread itself over the gastric mucosa more quickly than one ounce. Two ounces half an hour before the meal has still a better chance to cover the entire gastric mucosa, and consequently it may be argued a greater depression should be brought about. That the greater depression in the third instance is not due to prolonged treatment with oil is shown by the rapid rise of the HCl in the second control series to a point even higher than was reached in the first.

Case 9.—Mr. L. Hypersecretion with hyperchlorhydria.

EXPERIMENT 1a.

March 9, 1906.—Fasting stomach contained 20 c.c., free HCl 30, total acids 40. After lavage, patient ate a shredded wheat biscuit meal.

Time.	Quantity.	Free HCl.	Total acid.	Pepsin.	Pepsinogen.
7:55	Began eating.				
8:03	Finished eating.				
8:05	13 c.c.	Tr.	7.5 c.c.	0.1	0.6
8:10	13	12.5	15.	5.3	6.7
8:20	14	32.5	37.5	21.1	25.
8:30	12	35	42.5	1.75	
8:40	11.5	32.5	47.5	6.25	10.9
8:50	13	42.5	52.5	18.9	23.
9:00	12	40.	52.5	14.	18.9
9:10	11	35.	50.	16.8	25.
9:20	12	50.	60.	25.	14.
9:30	5	50.	60.	....	....
9:40	4.5	32.5	50.	14.4	
9:43	Lavage shows 5 free HCl.				

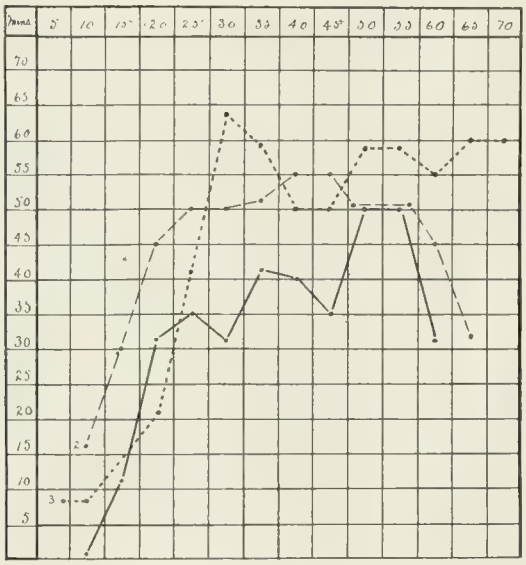

Chart 7, Case 9.—Mr. L. 1, solid line control; 2, line of long dashes, first oil meal, two ounces oil half hour before; 3, line of short dashes, second oil meal, three ounces oil half hour before.

EXPERIMENT 1B.

March 10, 1906.—Fasting stomach, 8 c.c., free HCl 25, total acid 39. After lavage the tube was allowed to remain in the stomach 6 minutes; 5 c.c. was now obtained showing free HCl 20, total acid 30. Peptic value of fasting stomach 41.5, and of the tube stimulation 16.

Time.	Quantity.	Free HCl.	Total acid.	Pepsin.	Pepsinogen.
8:10	Took 2 ounces olive oil.				
8:40	Began eating.				
8:43	Finished eating.				
8:50	7 c.c.	17.5 c.c.	38 c.c.	12.2	18.9
9:00	9.5	30	35	25	
9:10	10.5	45	60		

Time.	Quantity.	Free HCl.	Total acid.	Pepsin.	Pepsinogen.
9:20	11	50	65	25	
9:30	13	50	65	28	
9:40	12	52	70	16.8	18.9
9:50	10	55	70	7.8	
10:00	10	55	71	33.6	18.9
10:10	11	50	68	37.2	26
10:20	10	50	67	....	37
10:30	9	40	58	42.2	23
10:45	5	33	53	....	25
10:47	Lavage.	No free HCl.	5	16	9

EXPERIMENT 1c.

A third meal, given on a date not recorded. Fasting stomach gave 10 c.c., containing free HCl 46, and total acid 60.

Time.	Quantity.	Free HCl.	Total acid.	Pepsin P. V.
6:56	After lavage 3 oz. olive oil was given through a tube.			
7:25	Began eating.			
7:30	Finished eating.			
7:33	9 c.c.	8 c.c.	11	1
7:41	10	8	14	0
7:50	11			
8:00	11	21	38	
8:10	12.5	42	65	19.3
8:20	12	68	85	19.3
8:30	12	59	70	19.3
8:40	10	50	70	19.3
8:50	10	50	70	16
9:00	12	58	70	22
9:10	10	58	80	23
9:20	10	55	72	25
9:30	13	60	78	32.5
9:40	6	60	77	36

The stomach now appeared empty and as the patient was very tired no lavage was given.

SUMMARY.

	Digestive period.	Amount recovered.
Control meal	1:45	121 c.c.
First oil meal	1:65	118 c.c.
Second oil meal	2:15	148 c.c.

In this case there has been little or no depressant effect on the secretions from the oil. The second oil meal shows changes which simulate those in the preceding meals, a slow rise in the free acid as contrasted with the abrupt rise of the control, increasing gradually, with the exception of the 8:20 sample, toward the end of the digestive period, which has been distinctly prolonged. The factor of hypersecretion doubtless plays an important rôle in this case and will be considered later under that head.

SERIES II.

The following cases are those studied at the Craig Colony for Epileptics:

CASE 10.—No. 1416. Mr. H. E. W. Bad heredity. Epilepsy followed typhoid fever. Attacks of grand mal about once a week. No gastric complaints. The test meals consisted of two or two and a half ounces of bread and two glasses of water. Samples were taken every fifteen minutes.

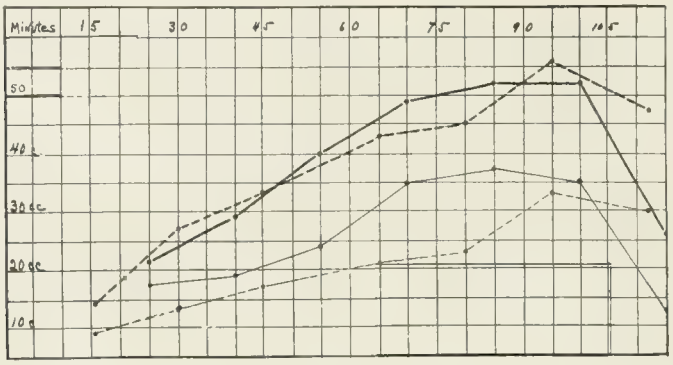

Chart 8, Case 10.—H. E. W. Experiment 1, heavy solid line, total acid of control. Heavy dashed line, total acid of oil meal. Lighter (and lower) dashed line, free acid of oil meal.

EXPERIMENT 1.

June 8, 1906.

Time.	Quantity.	Free HCl.	Total acid.
8:25	Began eating.		
8:48	Finished eating.		
8:50	20 c.c.	17.5 c.c.	21.5 c.c.
9:05	20	18.5	29
9:20	26	24	40
9:35	25	35	49
9:50	21	37.5	52
10:05	30	35	52.5
10:20	8	13.3	26.6

Free HCl, highest, 37.5, at 85 min. Amount recovered, 150 c.c.

June 9, 1906.—Same test breakfast as above.

Time.	Quantity.	Free HCl.	Total acid.
7:45	0.75 oz. cotton seed oil.		
8:20	Began eating.		
8:31	Finished eating.		
8:36	10 c.c.	9 c.c.	14 c.c.
8:50	25	13.5	22.7
9:05	30	17	33
9:25	25	21.5	43.5
9:40	25	23	45
9:55	24	33.4	56.2
10:12	5	30	47.5

Free HCl, highest, 33.4, at 95 min. Amount recovered, 144 c.c.

EXPERIMENT 2.

June 11, 1906.—Shredded wheat biscuit meal.

Time.	Quantity.	Free HCl.	Total acid.
8:24	Began eating.		
8:34	Finished eating.		
8:36	28 c.c.	3.7 c.c.	8.7 c.c.

Time.	Quantity.	Free HCl.	Total acid.
8:52	27	18.5	26
9:12	28	30	41
9:26	25	32	43
9:43	20	42.5	55
10:01	20	41	54
10:20	12	38	48
10:40	4	30	35

Highest free HCl, 42.5, at 79 min.; 164 c.c. recovered.

June 12, 1906.

Time.	Quantity.	Free HCl.	Total acid.
7:30	2 oz. oil per tube.		
8:02	Began eating.		
8:10	Finished eating.		
8:12	22 c.c.	6 c.c.	10.4 c.c.
8:28	20	8	17
8:43	30	24	33.5
9:03	30	34	46
9:20	20	46	58
9:36	20	43	57
9:53	10	..	..

Highest free HCl, 46, at 78 min. Recovered 152 c.c.

This patient had an epileptic attack about 7:30 a. m. preceding the control meal. He came to the laboratory at 8:15, complaining of a headache, and was slightly confused.

EXPERIMENT 3.

June 14, 1906.—Shredded wheat biscuit meal.

Time.	Quantity.	Free HCl.	Total acid.
8:25	Began eating.		
8:34	Finished eating.		
8:35	50 c.c.	7.5 c.c.	11 c.c.
8:50	20	22	33
9:05	20	40	52
9:20	20	35	48
9:35	20	50.7	61
9:50	10	57	67

Free HCl, highest, 57, at 85 min. Amount recovered, 140 c.c.

June 15, 1906.—Shredded wheat biscuit meal with oil.

Time.	Quantity.	Free HCl.	Total acid.
7:00	Oil, 2 oz.		
7:32	Began eating.		
7:38	Finished eating.		
7:40	15 c.c.	6 c.c.	11 c.c.
7:55	15	16	21
8:10	15	18	26
8:25	15	28	38
8:40	15	48.3	57.3
8:55	15	57	69
9:10	15	56.6	68.3
9:25	10	50	60

Free HCl, highest, 57, at 83 min. Amount recovered, 115 c.c.

EXPERIMENT 4.—DAILY MEALS.

Date.	Last seizure.	Quantity.	Free HCl.	Total acid.	
June 19	G. 9:40 p. m.				
June 20		150 c.c.	73 c.c.	86 c.c.	
July 5	G. 5 p. m.	90	66	80	
July 6		40	66	76	
July 7		110	54	68	
July 9		110	46	56	...
July 10		110	55	69.6	...
July 26		105	54	66	Oil.
July 27		38	50	62	Oil.
July 28		110	63	72	Oil.
July 29	G. 12:25 p. m				
July 30		12	60	88	Oil.
August 1		70	74	89	Oil.
August 2		90	56	65	...

Total number of daily meals, 12.

Average of 7 meals without oil, HCl, 59.4; total acid, 71. Amount, 100 c.c.

Average of 5 meals with oil, HCl, 60.8; total acid, 75. Amount, 67 c.c.

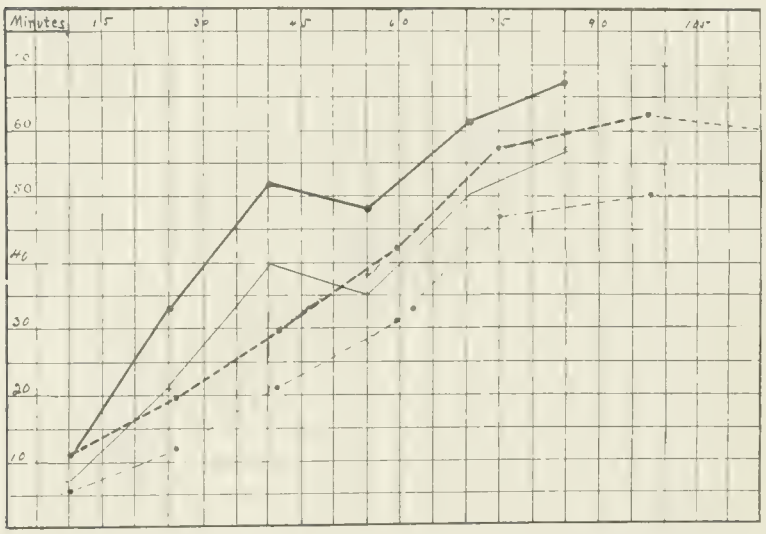

Chart 9.—Heavy solid line, total acid of control. Lighter solid line, HCl of control. Heavy dashed line, total acid for oil meal, being an average of experiments 2 and 3. Lighter (and lower) dashed line, HCl after oil meal, average of experiments 2 and 3.

SUMMARY.

In this case four experiments were conducted, three special meals and one series of daily meals. The results may be summed up as follows: There is distinct evidence of a depressant effect from oil in all of the special meals. With the control meals the rise of the HCl curve is quicker in all cases, except in Experiment 3. The rate of the secretion

is decidedly lowered by oil, being twenty minutes behind the control in Experiment 1 and about twenty minutes behind the control in Experiment 2. The height of digestion is reached at the end of the digestive period instead of the middle, as in the case of the control in Experiments 1 and 2, while in Experiment 3 practically no change can be noted.

Experiment 4 shows no depressant effect from the oil, but rather a reverse of what has been noted heretofore. In none of the experiments has there been any lowering of the motor power, and in Experiment 4 there seems to be a distinct increase in the motor power.

CASE 12.—Mr. W. Grand mal. No gastric symptoms. Test meals of dry toast and water.

EXPERIMENT 1.

Time.	Quantity.	Free HCl.	Total acid.
7:40	Began eating.		
7:45	Finished eating.		
7:55	22 c.c.	2 c.c.	8 c.c.
8:15	20	11.2	23.2
8:40	20	16	32
9:00	30	16	28
9:20	6	15	32.5

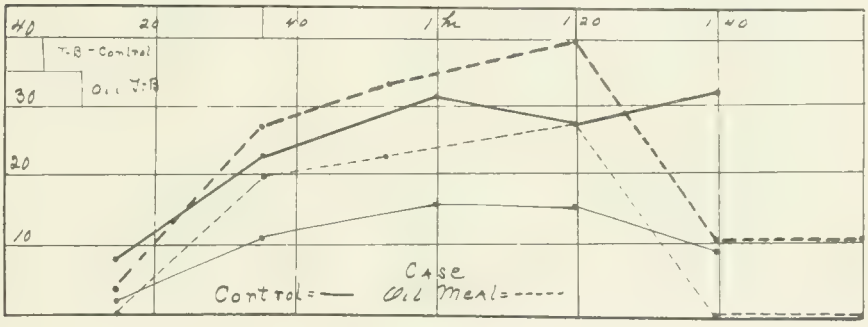

Chart 10, Case 12.

June 28, 1906.—Attack at 12:50 p. m.

Time.	Quantity.	Free HCl.	Total acid.
7:05	Oil given.		
7:40	Began eating.		
7:50	Finished eating.		
7:55	20 c.c.	0 c.c.	4 c.c.
8:15	20	20	27
8:33	20	23	34
9:00	20	27.5	40
9:20	20	Trace	12
9:40	15	0.0	12.5

EXPERIMENT 2.—DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	
June 23	90 c.c.	32 c.c.	44 c.c.	
June 26	55	38	48	
June 29	4	2	3	
July 3	200	8	16	Oil.
July 5	90	18	30	
July 6	?	26	36	
July 7	65	13	25	
July 9		10	20	Oil.
July 10	95	37	50	Oil.
July 26	18	00	..	Oil.
July 27	76	14	26	Oil.
July 28	80	16	27	

Average of 7 control meals: HCl, 20.7; total acid, 28; amount, 64.
Average of 5 oil meals: HCl, 14; total acid, 28; amount, 92.

SUMMARY.

Experiment 1.—The acidities with the oil were all distinctly higher than with the control. There is, however, a slowing of the rate of secretion in the oil meal, as well as a lowering of the motility. As the observations were made only at intervals of twenty minutes, the extent of the lowering of the rate of secretion can not be determined. The oil meal preceded an epileptic seizure by only a few hours. This may account for the increase in the acidities and the disappearance of the free HCl in the last samples.

Experiment 2.—Twelve meals were given in this series. There is distinct depression of the acidity from the oil and a lowering of the motility. If the averages are compared, distinct depression and decreased motility are noted. In the control meals, taken at random, there is a variation in the free acid values of from 2 to 32, while a corresponding change takes place in the total acid values. It is, therefore, impossible to maintain that the apparent depression in the oil meals is due to oil.

Attacks of the grand mal occurred June 24, at 12:15 p. m., and July 27, at 9:35 p. m. It may be noteworthy that the attack on June 24 was followed by almost complete absence of free acid, and that the attack of July 27 was preceded by a similar observation.

A case showing such wide variations is not suitable for experimentation. The record is presented here because the results of the special meal followed the general rule, showing a decrease in the rate of secretion with oil, and also because it may serve as an illustration of the possible outcome of observations taken at intervals so widely separated—ten days in one instance.

CASE 13.—Mr. A. H. Grand mal. No gastric complaints.

EXPERIMENT 1.

Probably June 17, 1906.

Time.	Quantity.	Free HCl.	Total acid.
8:52	Began eating.		
8:59	Finished eating.		
9:00	15 c.c.	0 c.c.	2 c.c.
9:20	15	8	12
9:35	15	13.5	20
9:50	20	12	34
10:05	17	27	38
10:17	20	18	29
10:36	20	20	32
10:57	35	38	54
11:12	15	22	35
11:27	15	12	24

EXPERIMENT 2.

June 18, 1906.

Time.	Quantity.	Free HCl.	Total acid.
7:00	Oil given.		
7:30	Began eating.		
7:36	Finished eating.		
7:40	15 c.c.	0 c.c.	4 c.c.
7:55	15	16	24
8:10	18	9	13
8:25	20	42	56
8:40	15	40	51
8:55	15	20	34.6
9:10	..	31	42.5
9:25	20	22	35
9:40	15	36.3	49.5
10:00	15	25	40

EXPERIMENT 3.

June 27, 1906.—Dry toast meal. Epileptic seizure the night before experiment.

Time.	Quantity.	Free HCl.	Total acid.
7:45	Began eating.		
7:52	Finished eating.		
8:00	20 c.c.	1 c.c.	4 c.c.
8:20	25	32	41
8:45	10	39	48

Stomach empty.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.	Seizures.
June 19	100 c.c.	60 c.c.	74 c.c.		
June 20	120	58	73		
June 21	45	46	60		
June 22	70	70	82		
June 23	55	64	74		
June 24	..	..	..		G. M., 11:35 p. m.
June 26	10	18	24		
June 28	20	12.5	75	Oil.	
June 29	10	26	42	Oil.	

Date.	Quantity.	Free HCl.	Total acid.	Oil.	Seizures.
July 3.....	110	9.9	22	Oil.	Attack before meal.
July 2 .	75	62	76		9th, 5:20 a. m.
July 10.....	90	27	42		
July 6.	10	50	90		
July 7	80	61	75		
July 9.....	25	56	66		
July 26	120	55	63		5:00 a. m.
July 28.....	78	26	42	Oil.	
Averages.—					
12 meals.....	66.6	55.5	70.6	No oil.	
4 meals.....	54	18.6	45	With oil.	

An inspection of the tables in this case shows that with the special meals the acidity was somewhat higher after the oil than after the control meals. The quantity recovered with oil is smaller than without.

The tests following daily meals show that with oil the quantity is somewhat decreased, while the acids are markedly lower than in control meals.

CASE 14. Mr. H. Grand mal.

EXPERIMENT 1.—SPECIAL MEALS.

June 22, 1906.—Samples taken every 15 min. No seizures.

Time.	Quantity.	Free HCl.	Total acid.
7:30	Began eating.		
7:36	Finished eating.		
7:40	20 c.c.	4 c.c.	8 c.c.
7:55	22	25	30
8:05	15	36	44
8:15	15	38	50
8:46	10	..	..

June 23, 1906.—Samples fifteen minutes apart.

Time.	Quantity.	Free HCl.	Total acid.
7:39	Oil given.		
8:00	Began eating.		
8:05	Finished eating.		
8:06	15 c.c.	10 c.c.	22.5 c.c.
8:20	20	16	27
9:15	Stomach empty.		

June 28, 1906.—Samples every twenty minutes. No seizures.

Time.	Quantity.	Free HCl.	Total acid.
7:05	Oil given.		
7:40	Began eating.		
7:50	Finished eating.		
7:55	20 c.c.	4 c.c.	8 c.c.
8:15	22	7	15
8:32	22	9	20
8:55	15	9	20
9:15	19	13.3	30

EXPERIMENT 2.—DAILY HOURLY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Seizures.	
June 26	19 c.c.	55 c.c.	66 c.c.	None.	No oil before.
June 27	8			None.	Oil before.
July 3	160	24	36	None.	No oil before.
July 5	100	48	64	None.	No oil before.
July 6	5	20	30	None.	No oil before.
July 7	75	69	85	None.	No oil before.
July 9	75	60	72	G.M., 6:40 a.m.	No oil before.
July 19	200	48	62	None.	Oil before.
July 27	..	16	27	None.	Oil before.
July 28	10	.		None.	Oil before.
July 30	280	Tr.	12	None.	Oil before.
July 31	20	20	32	None.	No oil before.
August 1	155	22	32	None.	Oil before.
Averages	47.5	45.3	58	Without oil.	
	116	22.5	34	With oil before the meal.	

This patient had epileptic seizures as follows: June 22, grand mal at 5:50 a. m.; June 29, grand mal, 10:40 p. m.; July 9, grand mal at 6:40 a. m.; July 29, grand mal at 12:50 a. m. It is of interest to note that on the day following the last seizure free HCl was present only in traces.

SUMMARY.—Experiment 1.—No depression is seen from oil in the first oil meal. The stomach emptied itself very quickly. The second oil meal shows a delay in the appearance of acid, a decrease in the amount at the height of digestion, and a prolongation of the digestive period, the height of which was reached at its end.

It will be observed that the average acidity of the oil meals was lower while the quantity recovered was increased.

CASE 15.—Mr. R. C. P. Epilepsy of unknown cause. Attacks of grand mal and petit mal. At one time there was an aura consisting of a sensation of cold in the stomach and a quickening of the heart. No gastric symptoms.

EXPERIMENT 1.

June 18, 1906.—Shredded wheat biscuit meal.

Time.	Quantity.	Free HCl.	Total acid.
7:54	Began eating.		
7:59	Finished eating.		
8:00	15 c.c.	0 c.c.	8 c.c.
8:16	15	4.6	12
8:30	15	14	20
8:45	15	0	10
9:00	15	16	25
9:15	15	10	16

June 19, 1906.—Shredded wheat biscuit and oil.

Time.	Quantity.	Free HCl.	Total acid.
7:00	Oil taken.		
7:32	Began eating.		
7:38	Finished eating.		
7:40	15 c.c.	0 c.c.	2 c.c.
7:55	15	0	6
8:10	15	0	0
8:25	15	2	6
8:40	15	10	20

EXPERIMENT 2.

Daily meals of shredded wheat biscuit until June 25, inclusive; toast meals thereafter.

Date.	Quantity.	Free HCl.	Total acid.	Oil.	Seizures.
June 20	90 c.c.	46.8 c.c.	58 c.c.	Control.	P.M., 1:20 p.m.
June 21	55	50	62	Control.	Mild, 2:40 a.m.
June 22	45	51	64	Control.	
June 23	12	51	64	Control.	
June 25	20	12	19	Control.	G., 10 p. m.
June 26	5	25	35	Control.	
July 3	190	8	16	Oil.	
July 5	40	30	40	Oil.	
July 6	80	56	66	Control.	
July 7	45	57	71	Control.	
July 9	35	25	44	Oil.	
July 10	..	17	35	Oil.	
July 26	148	11	20	Oil.	
July 27	58	31	41	Oil.	
July 28	2	10	20	Oil.	

Averages of 9 control meals: HCl, 39.8; total acid, 51; amount, 39.

Averages of 6 oil meals: HCl, 20.3; total acid, 32; amount, 94.

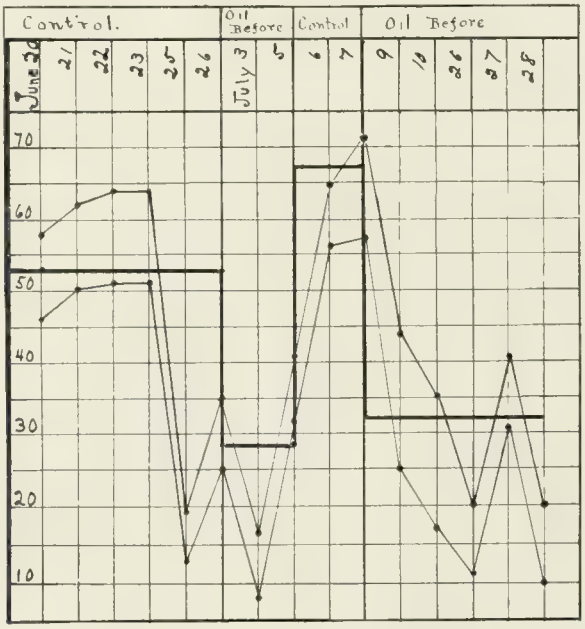

Chart 11, Case 15.—Experiment 2, heavy line, average total acid.

SUMMARY.

Experiment 1 shows what thus far seems to be the rule with the special meals, namely, a depression of the acidity by oil, a decrease in the rate of secretion, which continues at its height to the end of the digestive

period or reaches its highest point only at that time. The motility was unaffected by the oil.

Experiment 2.—Fifteen meals were given in this series, 9 without oil and 6 with oil. The secretion was distinctly depressed by the oil and the evacuation of the stomach lengthened.

Case 16.—Mr. G. S. Grand mal.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.	Seizures.
July 5	4 c.c.	20 c.c.	40 c.c.	Control.	
July 6	10	40	50	Control.	
July 7	5	17.5	30	Control.	
July 9	5	15	32.5	Control.	
July 10	10	22.5	32.5	Control.	
July 26	45	43.4	53.4	Control.	
July 27	8	0	..	Oil.	
July 28	10	5	10	Oil.	
July 30	8	10	20	Oil.	G. 1, a. m.
July 31	2	0	5	Control.	
August 1	9	14	20	Control.	
August 2	8	20	40	Oil.	G. 2, night.
August 3	8	Tr.	5	Oil.	
Averages.—					
Control	11.2	21.5	33		
Oil meals	8.4	7.0	19		

In this case attention should be called to the fact that up to the time of giving oil on the 27th, the lowest free HCl acidity was 15. The apparent effect of the oil was to reduce the secretion from 43.4 on the 26th to 0 on the 27th. On the 30th, following the administration of oil, the free acid was 10, while on the succeeding day without oil, its value was 0. On the next day free HCl reappeared and on August 2, notwithstanding the administration of oil, the record was a little higher.

Clinical and experimental experience tends to teach us that the effect of a dose of oil does not persist throughout the following day or even through the next meal. Its action seems to be limited to the period immediately following its administration.

When one considers these records the following questions arise:

(1) Was the low acidity found between July 27 and 30 dependent on nervous factors, and was its association with the administration of oil merely a coincidence?

(2) Was this low acidity, on the other hand, due to a true depressant action of the oil and were the low values of July 31 and August 1 the result of a persistence of one's depressing influence?

CASE 17.—Mr. L. R.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.	Seizures.
July 5.....	15 c.c.	34 c.c.	46 c.c.	Control.	July 5, 1 p. m.
July 7.....	35	33	51	Control.	
July [illegible]	40	37	54	Control.	
July 10.....	30	41	57	Control.	
July 26	8	53	63	Control.	July 25, 1 a. m
July 27.....	28	15	25	Oil.	
July 28	155	4	12	Oil.	
July 30.....	170	10	18	Oil.	
July 31.....	12	23	33	Control.	
August 1.....	130	18	25	Oil.	
August 2.....	30	11	26	Oil.	Aug. 3, 1 a. m.
Averages.—					
No oil.....	23	37	50	All attacks petit mal.	
With oil.....	102	12	21	All attacks petit mal.	

CASE 18.—Mr. C. M.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.	Seizures.
July 5.....	22 c.c.	40 c.c.	50 c.c.	Control.	
July 6.....	10	30	40	Control.	
July 7.....	120	48	65	Control.	
July 9.....	20	47	61	Control.	
July 10.....	145	37	51	Control.	
July 26.....	120	38	48	Control.	
July 27.....	50	30	50	Oil.	
July 28	240	0	6	Oil.	July 29, a. m.
July 30.....	..	29	41	Oil.	
July 31.....	75	40	54	Control.	July 31, a. m.
August 1.....	45	6	20	Oil.	
August 2.....	20	20	34	Oil.	
Averages.—					
No oil.....	40	51	71		Petit mal.
With oil.....	17	30	90		Petit mal.

In this series the control meals show free HCl values between 30 and 48, while the oil meals show a drop to below 30. The increase in the free HCl value on July 31 is of interest because oil did not precede the meal.

CASE 19.—Mr. F. K.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.	Seizures.
July 5.....	10 c.c.	6 c.c.	8 c.c.	Control.	G., a. m.
July 6	5	30	40	Control.	P., a. m.
July 7	15	44	58	Control.	
July 9.....	100	40	52	Control.	
July 10.....	8	5	12	Control.	P., a. m.
July 25.....	..	..	..		P., 25, a. m.
July 26.....	120	51	66	Control.	2 P., 26, a. m.
July 27.....	35	32	46	Oil.	P., 27, a. m.

Date.	Quantity.	Free HCl.	Total acid.	Oil.	Seizures.
July 28	40	0	10	Oil.	G., 28, a. m.
July 30	340	14	23	Oil.	
July 31	15	15	33	Control.	
August 1	80	58	70	Control.	
August 2	55	26	39	Oil.	P., a. m.
Averages.—					
No oil	44	31.0	85		2 G. mal.
With oil	107	18	29		6 P. mal.

CASE 20.—Mr. G. S.

Date.	Quantity.	Free HCl.	Total acid.	Oil.	Seizures.
July 5	15 c.c.	24 c.c.	42 c.c.	Control.	
July 6	42	50	70	Control.	P., a. m.
July 7	10	11	23	Control.	P., July 7, a. m.
July —	30	26	45	Control.	P., July 8, a. m.
July 10	15	11.6	25	Control.	P., a. m.
July 25					P., July 25, a. m.
July 26	30	27	39	Control.	P., July 26, a. m.
July 27	50	10	23	Oil.	
July 28	50	0	4	Oil.	
July 30	50	31	41	Oil.	
July 31	90	32	45	Control.	
August 1	25	31	46	Control.	
August 2	110	7	16	Oil.	
Averages.—					
No oil	32	26.5	42		
With oil	65	12	21		

CASE 21.—Mr. B. C.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.	Seizures.
July 6	55 c.c.	30 c.c.	40 c.c.	Control.	G. M.
July 7	120	19	38	Control.	
July 9	35	12	26	Control.	P. M.
July 10	75	21	39	Control.	
July 26	75	20	36	Control.	
July 27	100	6	20	Oil.	
July 28	60	14	26	Oil.	
July 30	200	6	18	Oil.	
July 31	115	22	34	Control.	
August 1	110	21	32	Oil.	
August 2	50	23	33	Oil.	
Averages.—					
No oil	79	21	35		
With oil	104	14	26		

CASE 22.—Mr. A. L. No seizures during experiment.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.
August 6	90 c.c.	33 c.c.	49 c.c.	Control.
August 8	50	37	52	Control.
August 9	45	29	44	Control.
August 10	45	28	46	Oil.
August 11	..	40	58	Oil.
August 13	36	20	35	Oil.
August 14	100	27	34	Oil.
Averages.—				
No oil	61	30	48	
With oil	60	29	46	

CASE 23.—Mr. H. Y. No seizures during experiment.

SUMMARY OF DAILY MEALS.

August 4	80 c.c.	23 c.c.	33 c.c.	Control.
August 6	30	36	47	Control.
August 7	30	34	45	Control.
August 8	25	32	43	Control.
August 9	72	9	16	Oil.
August 10	50	30	50	Oil.
August 11	170	10	23	Oil.
August 13	55	37	48	Oil.
Averages.—				
With oil	87	21	34	
No oil	41	31	42	

CASE 24.—Mr. R. W.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.	Seizures.
August 4	8 c.c.	15 c.c.	25 c.c.	Control.	G. M., a. m.
August 6	23	36.4	48	Control.	G. M., a. m.
August 7	60	60	78	Control.	G. M., a. m.
August 8	12	30	50	Control.	
August 9	12	6	20	Oil.	
August 10	15	20	36	Oil.	
August 11	20	20	37.5	Oil.	
August 12	..	..	..		G.M.,Aug.12, a.m.
August 13	10	17.5	32.5	Oil.	
August 14	..	..	..		G.M.,Aug.14, a.m.
Averages.—					
No oil	26	35.3	50		
With oil	14	16	31.5		

CASE 25.—Mr. W. C.

Date.	Quantity.	Free HCl.	Total acid.	Oil.	Seizures.
August 4	50 c.c.	19 c.c.	42 c.c.	Control.	
August 6	55	31	50	Control.	
August 7	22	20	34	Control	2 G. M., a. m.*
August 8	50	18	32	Control.	
August 9	35	11	23	Control.	
August 10	45	8	24	Oil.	2 p. m.
August 11	35	33	47	Oil.	
August 13	115	15	32	Oil.	
August 14	70	40	54	Oil.	
August 15	..	..	..		Aug. 15, 2 p. m.
Averages.—					
With oil	66	24	39		
No oil	42	20	36		

NOTE.—This case shows little change in the acidity, while after the administration of oil the evacuation is delayed.

CASE 26.—J. E. No. 1992. No seizures during experiment.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.
August 4	115 c.c.	34 c.c.	48 c.c.	Control.
August 6	30	16	35	Control.
August 7	95	34	55	Control.
August 8	4	15	30	Control.
August 9	12	14	32	Control.
August 10	12	22	38	Control.

Date.	Quantity.	Free HCl.	Total acid.	Oil.
August 11.	12	10	27.5	Control.
August 12.	15	?	20	Control.
August 14.	105	23	41	Oil.
August 15.	74	16	36	Oil.
August 16.	170	30	48	Oil.
August 17.	45	28	44	Oil.
August 18.	22	19	37	Oil.
Averages.—				
No oil	37	19	35.6	
With oil	83	23	41	

CASE 27.—R. B. No. 1045. No seizures during experiment.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.
August 4.	15 c.c.	8 c.c.	17 c.c.	Control.
August 6.	15	30	50	Control.
August 7.	10	16	27	Control.
August 8.	5	20	37.5	Control.
August 9.	8	30	50	Control.
August 10.	40	32	52	Oil.
August 11.	50	18	43	Oil.
August 13.	42	15	30	Oil.
August 14.	94	20	38	Oil.
Averages.—				
No oil	11	21	36	
With oil	56	21	41	

The oil had apparently no effect in this case except to decrease the motility.

CASE 28.—H. S. No. 885. No seizures during experiment.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.
August 5.	12 c.c.	40 c.c.	51 c.c.	Control.
August 6.	0	..	..	Control.
August 7.	20	38	50	Control.
August 8.	10	31	41	Control.
August 9.	10	10	16.6	Oil.
August 11.	125	10	35	Oil.
August 13.	15	0	5	Oil.
Averages.—				
No oil	14	36.3	47	
With oil	50	6	18.7	

CASE 29.—W. H. No. 1278. No seizures during experiment.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.
August 4.	40 c.c.	20 c.c.	32 c.c.	Control.
August 6.	80	24	40	Control.
August 7.	45	31	47	Control.
August 8.	35	30	43	Control.
August 9.	55	17	31	Oil.
August 10.	290	9	22	Oil.
August 11.	70	18	32	Oil.
August 13.	25	41	50	Oil.
Averages.—				
With oil	110	21	36	
No oil	50	29	40.5	

CASE 30.—W. M. No. 1096. No seizures.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.
August 6	20 c.c.	32 c.c.	54 c.c.	Control.
August 7	12	14	22	Control.
August 8	12	35	53	Control.
August 9	12	42	57	Control.
August 10	115	20	40	Oil.
August 11	165	20	33	Oil.
August 13	14	20	35	Oil.
Averages.—				
No oil	14	29.5	46.5	
With oil	98	20	35	

CASE 31.—F. K. No. 1889. No seizures.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.
August 4	28 c.c.	14 c.c.	29 c.c.	Control.
August 6	18	23	42	Control.
August 7	95	32	50	Control.
August 8	8	18	26	Control.
August 9	10	25	40	Control.
August 10	240	8	22	Oil.
August 11	290	13	27	Oil.
August 13	170	29	42	Oil.
August 14	35	16	20	Oil.
August 15	98	49	62	Oil.
August 16	135	42	54	Oil.
Averages				
With oil	161	26	38	
No oil	32	22.4	37	

CASE 32.—J. W.

SUMMARY OF DAILY MEALS.

Date.	Quantity.	Free HCl.	Total acid.	Oil.
August 6	5 c.c.	15 c.c.	30 c.c.	Control.
August 7	8	32	40	Control.
August 9	18	17.5	35	Control.
August 10	72	40	56	Control.
August 11	12	20	35	Control.
August 13	12	0	15	Control.
August 14	18	6	18	Oil.
August 15	42	17	28	Oil.
August 16	50	12	23	Oil.
August 17	82	9	23	Oil.
August 18	40	0		Oil.
Averages.—				
No oil	21	24.9	29.2	
With oil	48.4	10	33	

CASE 33.—Mr. A. K. (This case was overlooked and is not included in the summaries.)

EXPERIMENT 1.

June 20, 1906.

Time.	Quantity.	Free HCl.	Total acid.
7:45	Began eating.		
7:50	Finished eating.		
7:52	15 c.c.	2 c.c.	6 c.c.
8:05	15	16	26
8:24	20	25	36
8:48	16	43	58

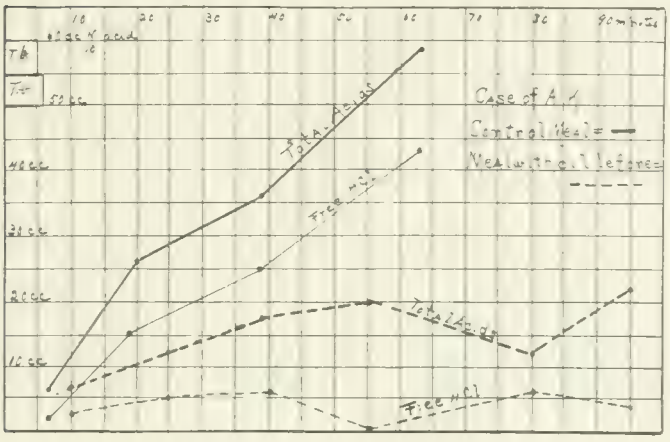

Chart 12, Case 33.—A. K.

EXPERIMENT 2.

June 21, 1906.

Time.	Quantity.	Free HCl.	Total acid.
7:00	Oil taken.		
7:30	Began eating.		
7:36	Finished eating.		
7:40	15 c.c.	2 c.c.	6 c.c.
7:55	20	5	12
8:10	15	5.4	17.4
8:25	15	0	20
8:50	15	6	12
9:05	20	4	22

A marked lowering of the acidity will be observed in the meal preceded by oil. On the next day, in 70 minutes, the free acid was 71 and the total acidity 87; on the 23d, 42 and 51. The diminution was therefore exactly coincident with the administration of oil.

The cases reported in the epileptic series were observed wholly by Dr. Munson. In connection with these cases, there were factors, the consideration of which will be taken up by him in a separate paper. The patients were all taking the bromid treatment, and, as this was a constant factor, we may assume that the effect, whatever it may have been, was constant. From a consideration of this series it would seem that an epileptic seizure does not exercise any definite influence on the gastric

secretion. At times a lowering of the acid values is observed before the seizure, while again a similar condition may follow the attack. When the cases of this series are taken collectively and considered critically, they are seen, for the greater part, to follow closely the rules established by the University Hospital cases.

The following table, comprising 310 stomach analyses of the daily meal series, has been compiled for the purpose of showing the average quantity and acidities of control meals, without oil, compared with meals preceded half an hour by oil:

TABLE 1.

Case.	Number of Meals.		Quantity.		Free HCl.		Total acid.	
No.	Control.	Oil.	Control.	Oil.	Control.	Oil.	Control.	Oil.
5	15	9	40	158	51	21	65	34
6	8	5	74	199	62.5	25.7	73	41
7	9	16	64	106	49	40.5	66.2	55
8	12	9	84	105	91	55.5	104.9	62.2
10	7	5	100	67	59	60.8	71	75
12	7	5	64	92	20.7	14	28	28
13	12	4	66	54	55.5	18.6	70.6	45
14	7	6	47.5	116	45.3	22.5	58	34
15	8	7	44	67.5	43.6	18.8	53.8	30.8
16	8	5	11.2	8.4	21.5	7	33	19
17	6	5	23	102	37	12	50	21
18	7	5	71	90	40	17	51	30
19	8	4	44	107	31	18	85	29
20	8	4	32	65	26	12	42	21
21	6	5	79	104	21	14	35	26
22	3	4	61	60	30	29	48	46
23	4	4	41	87	31	21	42	34
24	4	4	26	14	35.3	16	50	31
25	5	4	42	66	20	24	36	39
26	8	5	37	83	19	23	35.6	41
27	5	4	56	11	21	21	41	36
28	4	3	14	50	36	6	47	18.7
29	4	4	50	110	29	21	40.5	36
30	4	3	14	98	29.5	20	46.5	35
31	5	6	32	161	22.4	26	37	38
32	6	5	21	46.4	20.6	8.8	35	18.4
Averages of all meals			43.3	85.6	36.4	22.4	51.3	35.5

From the compilation of the averages of these 26 cases the following observations may be made:

(a) The motility was decreased in 18 cases,[9] increased in 5 cases,[8] unchanged in 3 cases.[10]

8. Cases 10, 18, 16, 24, 27.

9. Cases 5, 6, 12, 14, 15, 17, 18, 19, 20, 21, 23, 25, 26, 28, 30, 31, 32.

10. Case 22.

(b) The free acid was decreased in 19 cases,[11] increased in 0 cases, unchanged in 6 cases.[12]

(c) The total acidity was increased in 17 cases,[13] increased in 0 cases, unchanged in 8 cases.[14]

A true estimate of the action of oil on the gastric functions may be obtained by comparing the following averages of the 170 control meals with the 140 meals preceded by oil, for in these individual characteristics and modifying circumstances will be eliminated almost completely.

	Quantity.	Free HCl.	Total Acidity.
Controls	43.3	36.4	51.3
Oil meals	85.6	22.04	35.5

For this series of 310 meals, withdrawn one hour from the beginning of ingestion, it may be concluded that the administration of two ounces of oil, half an hour before the meal, delays the evacuation of the stomach and decreases the acidity markedly.

TABLE 2.

Case No.	No. of meal.	Beginning of secretion in the oil meals.	Free acid value of oil meal after 1 hr., compared with control.	Height of secretion reached in the		Ultimate height of secretion with the oil meals compared with controls.	End of secretion reached with	
				Control in min.	Oil meal in min.		Control in min.	Oil meal in min.
5	1	Delayed 10 min.	Decreased.	65	70	Lower.	85	90
	2	Unchanged.	Decreased.	65	85	Lower.	85	95
6	3	Delayed 10 min.	Decreased.	45	140	Higher.	75	140
9	4	Unchanged.	Same.	50	40	Same.	60	65
	5	Hastened.	Increased.	50	30	Higher.	60	70
10	6	Hastened.	Decreased.	85	95	Higher.	115	115
	7	Unchanged.	Increased.	79	78	Higher.	136	111
	8	Unchanged.				Higher.	110	113
12	9	Unchanged.	Increased.	85	83	Lower.	100	120
13	10	Unchanged.	Increased.	80	80	Higher.	155	150
14	11	Increased.	Increased.	125	55	Lower.	76	75
	12	Delayed 5 min.	Decreased.	45	20	Lower.	76	95
15	13	Delayed 31 min.	Decreased.	45	95	Same.	83	68
33	14	Delayed 5 min.	Decreased.	66	68	Lower.	63	95
			Decreased.	63	80			
Averages..		5 delayed.	8 decr.	4 hastened.		6 lower.	8 prolonged.	
		3 hastened.	5 incr.	7 prolonged.		6 higher.	2 shortened.	
		6 unchanged.	1 same.	3 unchanged.		2 same.	4 unchanged.	

In the special meal series a few additional points are demonstrated. An interpretation of the action of oil in producing the above effects is

11. Caoses 5, 6, 7, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 28, 29, 30, 32.

12. Cases 10, 22, 25, 26, 27, 31.

13. Cases 5, 6, 7, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23, 24, 28, 30, 32.

14. Cases 10, 12, 22, 25, 26, 27, 29, 31.

obtained. By referring to Table 2 and the acidity curves, it will be observed (1) that of the fourteen meals eight showed decreased acid values at the end of an hour, the decrease being marked in most cases and corresponding with the change noted in the daily meal series; (2) that in some cases the acidity reached its height earlier with the oil meals, but that in half of the cases the height of the secretion with the oil meals is markedly delayed as compared with the controls; (3) that the secretion period, or the period of digestion, is distinctly prolonged in eight of the fourteen meals.

There are many factors associated with experiments of this character which render it almost impossible to duplicate at all times the observations on the phenomena of digestion which may be made on dogs with isolated miniature stomachs. The psychic effects are altogether of an opposing nature, and the method of experimentation of necessity is radically inferior. The dog knows nothing about his miniature stomach and has only the most pleasurable psychic influences during his feeding, digestion and subsequent experimentation. In our cases the knowledge of experimentation and the discomfort caused by the presence of the tube in the stomach, or by its frequent passing, are constantly present. Under such conditions there are certainly no appetizing influences at work and consequently little or no psychic juice, which seems to figure so largely in Pawlow's experiments, is secreted.

When, under ideal conditions, the administration of oil to dogs with miniature stomachs brings about lowered acidity values, delay of the height of digestion, lengthening of the digestive period and lowering of motility, and when experiments on the human stomach are followed, in a large proportion of cases, by results which closely simulate other dogs, it would seem only logical to conclude that the conditions observed in the dog's stomach are closely analogous to those which occur under similar conditions in the human being.

Such results as were obtained in Case 6 and Case 9 are influenced by a factor which in the one case (6) was not always at work, while in the other (9) it was constant, namely, the factor of hypersecretion. In the former case our examinations showed intermittent hypersecretion; in the latter continual hypersecretion, for in this case the fasting stomach always contained a strongly active gastric juice.

Our experiments show that, when once the secretion is induced, its progress is not easily influenced by oil. At times, in hypersecretion, even though the precaution be taken to wash and drain the stomach, only a few seconds will suffice to enable one to collect a sample of gastric juice of decided peptic value (Case 6). If, on the other hand, the fasting stomach contains no gastric juice and oil be introduced, the characteristic

group of digestive phenomena are almost invariably observed, namely, delayed secretion, retardation of the appearance of the height of digestion, prolongation of the digestive period.

DISCUSSION.

We have definitely confirmed the observations of others and proved that oil produces a certain group of gastric phenomena which are spoken of as depressant. The question as to how this is brought about appears to us to have been unsettled up to the present time. As cited in our introductory remarks, Pawlow maintains that the influence of fats and oils is exercised through reflex central stimulation of the inhibitory nerves of the glands or the inhibitory centers of these nerves; that it is not the result of their purely mechanical action in covering the mucous membrane and preventing excitation of the nerve endings. Later he admits that the mechanical effect has not yet been satisfactorily shown. Pawlow's experiments are conclusive that oil does have a central inhibitory action. But, we think, the purely mechanical effect of oil plays a great, if not as great, a part in lowering the acidity of peptic digestion.

It has long been known that certain kinds of food remain in the stomach longer than others, and that the evacuation of the stomach, as well as its secretion, is subject to food stimulation. If food, coated with oil, cannot stimulate the gastric nerve endings, no juice will flow until, by mechanical effect, the oil is removed from certain portions of the food. We may then consider that oil acts mechanically in two ways: (1) by covering the food; and (2) by covering the mucosa. We bring forward two experiments which seem to sustain these views. If three pieces of coagulated egg albumin of the same size be immersed for a few minutes in water, glycerin and olive oil, respectively, and then placed separately in tubes containing equal amounts of stomach fluid and incubated at body temperature, it will be observed that by the time the control has been completely dissolved, which occurs with comparative rapidity, the glycerinized piece is about one-half digested, while the piece immersed in oil is only beginning to show the slightest change around the edges. It is quite apparent from this experiment that oil interferes with digestion by coating the food and mechanically preventing the digestive juices from attacking it.

The fact that oil, given immediately before or after a test meal, does not bring about so marked a lowering of the secretions as when it is given half an hour before, leads one to believe that there are more than reflex central inhibitory influences at work. Food stimulation, as well as psychic stimulation of nervous mechanisms, is usually more

promptly induced. Two ounces of olive oil administered ten minutes before a meal depresses the secretion more than does one ounce, but not as much as when it is given thirty minutes before the meal.

To see if this mechanical phenomenon could be shown graphically, the following experiment was conducted in the Radiographic Department of the University Hospital. Our thanks are due Mr. Vernon J. Willey, director of the laboratory, for giving freely of his time, and for the excellent radiographs made.

Two ounces of olive oil, intimately mixed with one ounce of bismuth subnitrate, were given to a very thin patient with slight gastroptosis. The patient was strapped to a plate and two minutes after swallowing the mixture an exposure was made. Another plate was exposed at ten minutes, another at fifteen, and still another at twenty-five minutes. In the first plate the oil and bismuth appears as a roundish or oval mass lying at the bottom of the stomach. As the time progressed an increase in the area of coating occurred, until at twenty-five minutes the entire stomach was coated.

From this experiment, particularly when taken in conjunction with Case 8 and the preceding experiment, it can be asserted that olive oil delays the secretion of the gastric juice to a considerable extent, at least by mechanically coating the walls of the stomach.

Taking all facts into consideration, the following conclusions appear to be justified:

1. Oil depresses the secretions of the stomach by reflex central action.
2. The reflex action is unlike that of ordinary food stimulation in that it is slower.
3. The reflex central action is a quantitative one, the depression becoming greater as the amount of oil administered is increased.
4. Oil depresses the secretion of the gastric glands by mechanical inhibition of food stimulation: (a) by coating the food; (b) by coating the stomach wall.
5. In proportion to the rapidity with which the walls of the stomach are covered with oil, the inhibition of secretion occurs, from nervous as well as from mechanical influences.

Our experiments lead us to the opinion that the characteristic group of phenomena which follow the administration of olive and cotton seed oil are due to mechanical action as well as to reflex, central, inhibitory stimulation.

Much knowledge can be obtained from experiments of this character. Such experiments, though laborious and beset with numerous factors of error, are entirely feasible. Although the results compare closely with

those acquired by animal experimentation, still it would seem advisable to proceed along some such line as this and investigate the action of all food stuffs, as well as of such drugs as are supposed to influence gastric secretion. A trustworthy control and a suitable subject are the all-important requirements. In the University Hospital cases hyperchlorhydria was present. In the Craig Colony cases the secretions were for the greater part within what we call the normal limits. Normal cases would probably form a more ideal basis of investigation from a purely experimental point of view.

CONCLUSIONS.

1. Olive oil and cotton seed oil, when given in connection with the usual test breakfast, decrease the gastric acidity at the end of the hour and retard the evacuation of the stomach.

2. The beginning of the secretion of hydrochloric acid is delayed when oil precedes the meal, unchanged when oil follows the meal.

3. The height of digestion is delayed when oil is given either before or after the meal.

4. The height of secretion is lowered when oil precedes the meal, unchanged when oil follows the meal.

5. If the progress of digestion is watched by the removal of small samples of stomach fluid at frequent intervals it will be observed, when oil precedes the meal by one-half hour, that at the end of what is usually taken as the digestive period for a test breakfast (three-fourths to one hour) the acidity is distinctly lower, while as great a height as is present in the control meal is frequently reached some minutes later.

6. The action of oil on the stomach functions is only a temporary one. It has no effect on subsequent meals unaccompanied by oil.

7. The therapeutic value of oil is apparent. In *suitable* cases it is preferable to antacids because of its caloric value. In hyperchlorhydria it should precede the meal. In hypochlorhydria it should follow the meal. In stasis and persistent slow evacuation it should be eschewed. In hypermotility it may be given before, during or after the meal.

8. Oil lowers the gastric secretion both by reflex central inhibitory stimulation and by mechanical action.

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EXPERIMENTAL AND CLINICAL INVESTIGATION OF THE PULSE AND BLOOD PRESSURE CHANGES IN AORTIC INSUFFICIENCY.*

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INTRODUCTION.

Although the collapsing pulse has, since the time of Corrigan, been one of the most characteristic features of aortic insufficiency, and although in its exaggerated form it furnishes the most typical of all pulse tracings, nevertheless one is struck by the frequency with which the sphygmograph produces a seemingly normal tracing in cases of perfectly definite aortic insufficiency where the sensation to the finger is that of a collapsing pulse. Usually it has been considered that such tracings are the result of instrumental defect or imperfect technic in making the tracings, and in a few cases they are ascribed to a simultaneous occurrence of aortic stenosis along with the insufficiency.

The discrepancy between the sphygmographic tracings and the subjective notes is well exemplified in the examination of the records of patients observed in the Johns Hopkins Hospital during the past four years, in which the pulse was described and the description accompanied by a sphygmographic tracing. Of 50 such records of cases of aortic insufficiency, in 58 per cent. the pulse was stated to be collapsing, while in the remaining 42 per cent. it was described as being gradual in its fall or non-collapsing.

The large proportion of cases which do not present a collapsing pulse is a point of great importance, and will be referred to later. The rapidity of the upstroke, which is constantly referred to by authorities as one of the leading features of the pulse, varied so little in the various tracings that it was impossible to utilize it as a standard whereby the two types of pulses could be compared. Advantage was taken, however, of that other characteristic of the sphygmogram, viz.: the low position of the dicrotic notch on the catacrotic limb as the criterion for comparison. In all but two cases, in which the pulse was described as non-collapsing, the notch was situated above a line drawn parallel to the abscissa, and midway between it and the apex. In those cases described as collapsing,

* Thesis presented for the degree of M.D. of the University of Edinburgh, April 31, 1907. Awarded gold medal and authorized for publication.

no such definite relation existed, for in those in which the amplitude of the pulse wave was great it was situated below this line, while in those in which the pulse wave was small it assumed a position above it, and the tracing partook of all the characters of a normal pulse.

Examples of these different types of pulse in aortic insufficiency are seen in Figures 1, 2 and 3.

Fig. 1.—Pulse described as non-collapsing. The dicrotic notch is situated above the line midway between apex and trough of the waves. Case of uncomplicated insufficiency. Systolic blood pressure, 160. Diastolic blood pressure, 70.

From the explanation hitherto advanced, that collapse of the pulse in this disease results from regurgitation, it is difficult and indeed impossible to account for the absence of the collapsing pulse in the large percentage of cases mentioned above. The explanation which would first suggest itself would be that the leak was small in degree and insufficient to render the vessels flaccid. The intensity of the diastolic murmur at the base of the heart, or the extent of cardiac hypertrophy and dilatation being no absolute gauge of the amount of blood which regurgitates

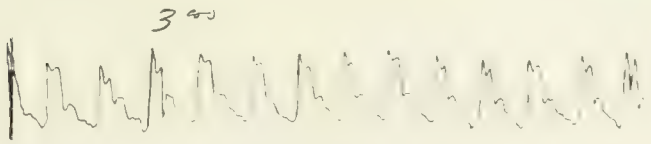

Fig. 2.—Pulse described as collapsing. The dicrotic notch is below the midline. Systolic pressure = 150. Diastolic pressure = 60.

into the ventricle, it was only from those cases which came to autopsy that information could be gathered on this point. Of the 21 cases which during life presented evidence of aortic insufficiency without a water-hammer pulse, 6 were examined postmortem. Four had varying degrees of arteriosclerosis. In 3 autopsies, the cusps were not so described that conclusions could be reached as to their actual incompetency. In the other 3, however, the valves were stated to be markedly shrunken and incompetent (without any accompanying stenosis). It is clear, then,

from these facts that distinct inadequacy of the aortic valves can exist without any accompanying water-hammer pulse, and its absence must be due to some other condition of the circulation.

The explanation will be proved experimentally to be that which was surmised by Sansom.[1] He recognized two types of pulse in aortic insufficiency. One in which the rise and fall are sudden, and a second in which there is "a resemblance with the tracings indicating high tension." In describing the latter class, he says: "The summit of the trace is broadened, the tidal wave being sustained, the dicrotic notch, though ill pronounced, is high in the tracing, and the gradually sloping line corresponding to the diastolic period tells of peripheral obstruction." The question, then, naturally arises, When shall a pulse be considered collapsing? Simple as this question at first sight seems, we are confronted at once with some difficulty in answering it. For, according to MacKenzie[2] and Broadbent,[3] the most distinctive feature of a collapsing

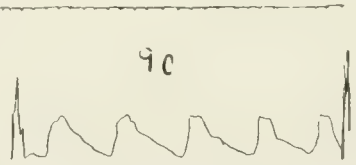

Fig. 3.—Pulse described as collapsing. The amplitude is small and the dicrotic notch is situated above the midline. Apparently a normal pulse tracing. Systolic pressure = 110. Diastolic pressure = 60.

pulse is, in effect, the fact that while in the normal radial pulse the dicrotic notch falls nearer the summit than the trough of the pulse wave (i. e., above the line drawn midway between summit and trough), in the collapsing pulse it is to be found below this line. In other words, the greater portion of the fall in the collapsing pulse occurs before the dicrotic notch, while in the normal pulse it occurs after it. Now, since Huerthle[4] has proved that the dicrotic notch divides the pulse tracings into two portions, the systolic occurring before the notch and the diastolic occurring after it, it is but a paraphrase to restate the criterion of MacKenzie and Broadbent by saying that *in the normal pulse the greater portion of the fall in the pulse wave is diastolic in time, while in the collapsing pulse of aortic insufficiency the greater portion of the collapse* (occurring before the dicrotic notch) *is systolic.*

1. Diagnosis of Diseases of Heart, London, 1881, p. 290.
2. Study of Pulse.
3. The Pulse, p. 205.
4. Arch. f. d. ges. Physiol., Bonn, 1891, xlix, 65.

In other words, if MacKenzie and Broadbent are correct, the greater part of the collapse occurs, not at the time when blood should be leaking back into the ventricle, but while it is still flowing from the ventricle into the aorta, during systole. The authors themselves do not attempt to explain this paradox; in fact, they do not even appear to realize its existence.

We are, therefore, confronted with the following problems:

First.—To investigate the substantial truth of the statement of MacKenzie and Broadbent, that the dicrotic notch occupies a low position in the pulse curve of aortic insufficiency. In other words, to determine whether the main fall of pressure is systolic or diastolic in time.

Second.—To determine the condition to which the main fall of pressure in aortic insufficiency is due.

In order to solve these problems, I have made numerous observations on patients in the medical service of Prof. L. F. Barker, in the Johns Hopkins Hospital, Baltimore, and I have performed many experiments on animals in the physiologic laboratory of the Johns Hopkins medical clinic, which is under the charge of Dr. A. D. Hirschfelder.

I would take this opportunity of expressing my warm thanks to Professor Barker for the many privileges which he has in so generous a manner extended to me while attending the medical clinic of the Johns Hopkins Hospital. Through his kindness I was enabled to utilize the clinical material under his charge and at the same time to carry on experimental work in the physiologic laboratory of his clinic.

I am also under a debt of gratitude to Dr. Hirschfelder. The experimental part of this research was carried out under his guidance, and my obligations are heartily acknowledged for the untiring assistance and valuable advice which he has at all times given me.

HISTORICAL SUMMARY.

While to Hodgkin[5] may be ascribed the distinction of being the first to give a clinical description of this disease, it was reserved for Corrigan[6] to offer, three years later, in 1832, an explanation of its most prominent features.

He recognized in the pulse only the grosser qualities of throbbing and pulsation. In his original article the following description is given:

"When the semilunar valves . . . become incapable of closing the mouth of the aorta, then, after each contraction of the ventricle, a portion of the blood just sent into the aorta, greater or less according to the

5. London Med. Gaz., 1829, iii, 433.
6. Edinb. Med. and Surg. Jour., 1832, xxxvii, 225.

degree of inadequacy of the valves, returns back into the ventricle. Hence, the ascending aorta and arteries arising from it, pouring back a portion of their contained blood, become, after each contraction of the ventricle, flaccid or lessened in their diameter. While they are in this state the ventricle again contracts and impels quickly into these vessels a quantity of blood which suddenly and greatly dilates them. The diastole of the vessels is thus marked by so sudden and so great an increase of size as to present the visible pulsation which constitutes one of the signs of the disease."

Corrigan was conscious of the fact that the backward current of blood could not sufficiently account for the appearance of the collapse in the arteries of the lower limb, or of the arm when dependent, since the blood would have to flow upward in its return to the aorta, and to render this possible he says: "The elasticity of the brachial arteries on the blood just urged into them forces it back along the retrograde current of the subclavians, no obstacle meeting it in that direction." He considered that the strength of the heart had little to do with the result, and that the explanation lay in the wave of large amplitude which was thrown into the empty artery.

Galabin,[7] forty years later, laid stress on the quality of extreme suddenness in the commencement of the pulse, which gives to the finger the sensation of a sudden jar or knock. He considered that this is the diagnostic quality of the pulse wave of aortic insufficiency, and pointed out that the amplitude of the wave itself is not characteristic, unless it is accompanied by the sudden jar.

This suddenness he attributed, not to an increased rate of systolic output, but to conditions in the vessel which altered the character of the pulse wave as it travels from the heart to the periphery. He maintained that the collapse did not exist in the larger arteries, such as the aorta and subclavian, but that the transformation which is seen in the wave as it traverses the peripheral vessels, is only an exaggeration of a change in the pulse form which takes place in the healthy adult. He showed that the rate of transmission of the pulse wave is dependent on the tension of the arterial walls, it being greater as the tension rises. Since the tension on the arterial walls is greater at the summit than at the trough of the pulse wave, the apex tends to overtake the base. The result is that the systolic elevation becomes steeper the further the wave travels from the heart. According to Galabin, in the normal pulse this tendency toward increased steepness of the systolic elevation is counter-

7. Trans. Roy. Med. and Surg. Soc., London, 1876, lix, 361.

acted by the recoil of the arterial walls, and as the influence which tends to make this upstroke steeper is the difference between the systolic and diastolic pressures, the conditions are established in aortic insufficiency for its production.

However faulty Galabin may have been in his reasoning, there is no doubt that he has the credit of being among the first to emphasize those qualities which we now imply with reference to the waterhammer pulse. These are the sudden, abrupt rise of the pulse curve and its rapid subsidence.

Clifford Albutt[8] introduces a new factor into the conditions which cooperate in the production of the collapsing or water-hammer pulse. The great changes of pressure which occur between systole and diastole have the effect of lengthening and widening the vessel, so that the walls adapt themselves but loosely to the blood which they contain. The arteries are thrown into curves, which on being straightened by each ventricular systole cause the vessel to be thrown out of its bed "with a visible and palpable jerk." That this contributes to the sensation of a jar or shock is undoubted, but it can not be the sole cause, for the water-hammer pulse can be distinctly seen before the vessels have had time to elongate, as is seen to follow the recent rupture of an aortic cusp.

With the exceptions already stated, our conceptions regarding the collapsing pulse have undergone no fundamental change since the publication of Corrigan's article, and while the blood pressure changes have been extensively studied in experimental aortic insufficiency by Cohnheim,[9] Romberg and Hasenfeld,[10] Kornfeld[11] and Rosenbach,[12] the underlying factors in the production of the collapsing pulse either are not mentioned by them or are assumed to be the direct consequence of regurgitation.

Among clinicians, some of the more recent authorities incline more to the emptiness of the arteries as the essential factor in its production (Gibson[13]), while others maintain that the sudden drop of the pulse wave is due to the loss of support from defective valves (Mackenzie[2]). The pervading idea is that the collapse occurs in the diastolic phase of the cardiac cycle, and that it is a direct consequence of regurgitation into the ventricle.

That the collapse is not diastolic, but occurs during ventricular sys-

8. System of Med., vi, 937.
9. Lect. on Clin. Path., New Syd. Soc., 1889, i, 49.
10. Arch. f. Exp. Path. u. Pharmakol, Leipz., xxxix, 333.
11. Ztschr., f. klin. Med., Berl., xxix, 91.
12. Arch. f. Exp. Path. u. Pharmakol., Leipz., ix, 1.
13. Diseases of Heart and Aorta, 183.

tole, and that it is only a secondary accompaniment of regurgitation, the evidence here advanced will prove.

METHODS OF INVESTIGATION.

The experimental part of this research was performed on dogs. It was found, after the first few experiments were performed, that the most suitable animal was a medium-sized English terrier, if possible over 2 years old. Young dogs were unsatisfactory, in that they did not appear to possess the same resistance as the older dogs and succumbed early in the experiment, owing to the severity of the cutting operation.

Each animal received ½ grain of morphia before being anesthetized with ether. This was administered by means of a tracheal cannula in connection with an ordinary ether bottle. After the thorax was opened, this was attached to an artificial respiration pump, and by the suitable adjustment of valve and T-tubes the lungs could be filled to any desired extent.

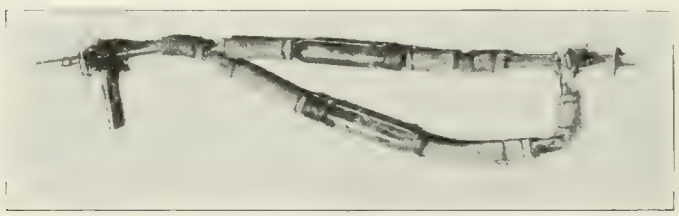

Fig. 4.—Dawson's maximal and minimal valves.

The pulse wave was recorded with a Huerthle membrane manometer, attached to the right carotid artery. Fling of the lever was eliminated by damping the movement with the screw lock of the apparatus.

The systolic and diastolic pressures were measured by the use of the maximal and minimal valves devised by Dawson[14] (Fig. 4). The more minute details are shown in Figure 5.

Each consists of two glass tubes, one enclosed within the other. The orifice of the inner tube, which is situated laterally, is surrounded by a layer of peritoneal membrane, so arranged as to permit the flow of fluid from within outward. When the inner tube A is attached to the artery, and the outer B to a mercury manometer, as in the upper figure, the systolic or maximal pressure only is recorded, the pressure in the outer tube being maintained by the membrane which closes the orifice C of the inner tube, when the pressure falls during diastole. By connecting the

14. Amer. Jour. of Physiol., Boston, 1906, xv, 224.

tube B with the artery and A with the manometer, the valve measures the minimal or diastolic pressure. The systolic rise of pressure now closes the orifice C, while the diastolic fall makes the pressure in the outer tube less than that which is in the inner, and thus causes a flow of fluid from the manometer toward the artery. By a suitable arrangement of stop-cocks (see photograph), the maximal valve is first connected with the artery, and having read off the systolic pressure on the manometer, it is cut off and the minimal or diastolic valve brought into communication with the artery.

In order to render the tracings less complicated, the systolic and diastolic pressures were read off and not recorded on the drum. It is to be noted that these valves do not record the systolic and diastolic pressures

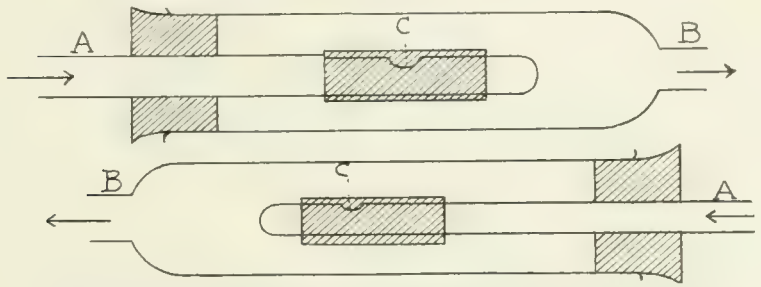

Fig. 5.—Minute details of Dawson's maximal and minimal valves.

of individual pulse waves. They measure the highest and the lowest pressures which have obtained in a given interval of time. If, however, this interval of time is made as short as possible, they will give records, which, for all practical purposes, are the systolic and diastolic pressures of the beats which occurred while the reading was being taken.

The amount of systolic output and the different phases of the cardiac cycle were recorded by the ventricular plethysmograph devised by Henderson[15] (Fig. 6).

It consists essentially of an ordinary soft rubber ball into which a circular window is cut, having a diameter of seven-tenths that of the ball. Over this window a very thin rubber dam is cemented with rubber cement, and after this has dried thoroughly a second circular window is cut into the rubber dam, this window having six-tenths the diameter of the window in the ball. A small hole is then cut into the side of the rubber ball, and through it a small glass tube is inserted and held in place with washers of cork or rubber. The apex of the heart is then

15. Amer. Jour of Phys., 1906, xvi, 325.

inserted into the window in the dam, and the plethysmograph pushed over the heart until the rubber dam fits about the auriculoventricular groove. The fitting should be airtight, but never sufficient to compress the heart. As Henderson states, it is necessary to have several sizes of the plethysmograph, and balls of diameters of 7, 9 and 11 cm., respectively, were used, according to the size of the heart. By its opposite end the plethysmograph communicates by rubber tubing with a large Marey tambour. The superiority of this instrument over that of Roy and Adami and the older forms lies in the fact that it registers the volume changes of the ventricles only, and, the transmission being by air, the ventricles are subjected to no external pressure which would impede their diastole.

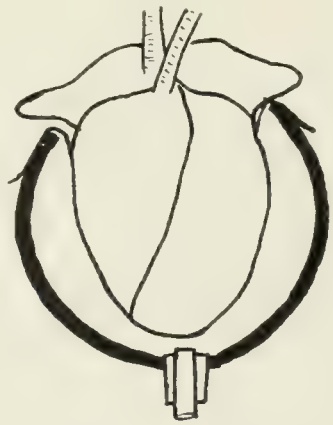

Fig. 6.—Henderson's ventricular plethysmograph in position.

After each experiment, the tambour was calibrated by attaching it to the upper end of a graduated burette filled with water. One cubic centimeter of water was run out at each time, and the excursion of the lever recorded.

After the insertion of the tracheal cannula, the internal mammary arteries were ligatured in order to avoid hemorrhage when the chest was opened. This was done by prolonging the incision for the preliminary tracheotomy to the upper border of the sternum, and separating the suprasternal muscles. The pleuræ were then punctured by the finger and, having dissected the arteries with the finger, a ligature was passed around them with an aneurism needle and then the ligatures tied.

The heart was exposed by reflecting the skin and pectoral muscles by a median incision extending along the whole anterior aspect of the chest. The ribs were cut near their attachments to the cartilages, and the ster-

num and costal cartilages removed. The pericardium was incised and reflected, and the plethysmograph slipped over the ventricles, until the rubber membrane grasped the auriculoventricular groove.

The aortic valves were ruptured by MacCallum's valvulotome.[16] This instrument (Fig. 7) consists of a steel cutting hook which is passed down the left carotid artery. The cutting surface is on the concave

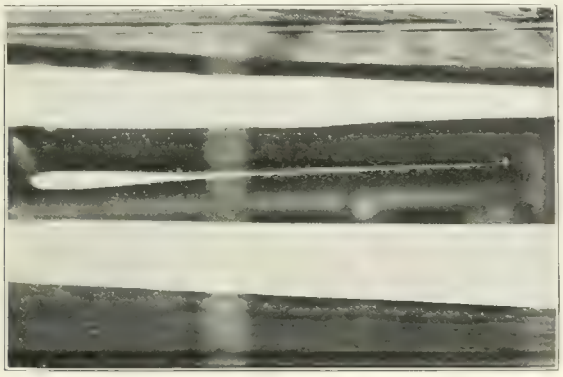

Fig. 7. —MacCallum's valvulotome.

aspect of the hook, which is so curved that it does not injure the vessels when passed down toward the heart. The instrument is pushed down the artery until it enters one of the sinuses of Valsalva, after which it is forced through the base of the cusp. The hook is then pushed inward, and, on being withdrawn, it cuts the cusp in two.

Intraventricular pressure was measured by means of a metal catheter passed down the left carotid artery and connected with a Huerthle manometer (Fig. 8).

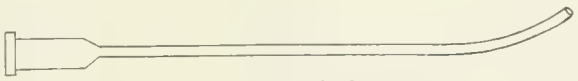

Fig. 8.—Intraventricular sound.

The changes in auricular pressure were recorded by passing a glass cannula into the auricle through a pulmonary vein and connecting this with a Harvard membrane manometer.

For the arterial, intraventricular and auricular pressures, the medium of transmission was a 5 per cent. solution of sodium citrate.

The heart of the animal was examined at the termination of each experiment, and only in those cases in which the valves were torn were

16. Johns Hopkins Hosp. Bull., Balt., No. 185, 1906.

the results put on record. In several cases, it was found that, in addition to the production of insufficiency, the intraventricular septum and the chordæ tendinæ were injured. The results of these experiments were not taken into account. In all, thirty experiments were performed, of which ten were successful, i. e., the aortic valves only being injured. In 9 the myocardium had been more or less damaged. In the remainder no insufficiency was obtained.

Methods of Recording.—Simultaneous tracings were made of the pulse changes, the volume changes of the ventricles, and of the time in fifths of a second with a Jacquet chronograph. In the earlier experiments smoked paper was employed, but in the later ones, by the use of improved writing pens, it was found that black on white tracings were

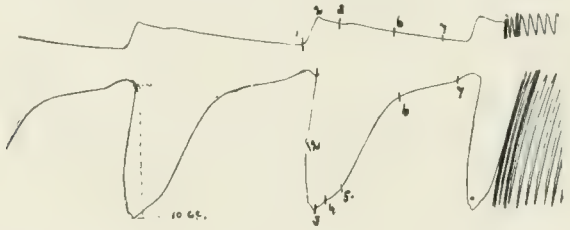

Fig. 9.—Simultaneous tracing of the pressure in the carotid artery (upper curve) and of the volume changes in the ventricle (lower curve): 1. Commencement of ventricular contraction. 2. Summit of primary wave. It is reached about the time that the ventricle has discharged half its contents into the aorta. 3. End of systole. It corresponds to the dicrotic notch in the carotid tracing. 3-4. The rapid increase in volume due to the filling of the coronary arteries. 5. End of relaxation or diastole proper. 6-7. Period of diastasis. 7. Commencement of auricular systole. The contraction of the auricle takes place after the ventricles have practically filled. It causes only a slight rise in ventricular volume. The downstroke 1-3 indicates a systolic discharge of 10 c.c.

more satisfactory. In every case, before and after a tracing was taken, the maximum and minimum blood pressures were read off. Typical normal tracings were always obtained before the aortic valves were injured.

THE VENTRICULAR VOLUME CURVES OF THE NORMAL HEART.

The results obtained by Henderson[15] are of such far-reaching importance that they mark a new era in our conceptions regarding the mechanism of the circulation in the normal heart. And, if true of the normal heart, they must modify to a still greater extent our views concerning the changes which occur in the circulation as a result of incompetency of the aortic valves. As one of the main arguments of this research is based on these results, his experiments have been carefully repeated, and the findings are in entire accord with those which he has obtained.

Figure 9 is a simultaneous record of the volume curve and the lateral pressure in the aorta as measured from the right carotid artery. After making allowance for the time taken by the pulse wave to reach the carotid artery, the figures represent simultaneous events in the two tracings. It will be seen that the greater part of the downstroke of the volume curve is practically a straight line, indicating a uniform rate of systolic discharge. Keeping in view the fact that the lever carrying the pen writes in the arc of a circle, the lower part of the systolic downstroke is seen to be more gradual, showing that toward the end of systole the discharge is less rapid; 3 indicates the end of systole and the commencement of ventricular relaxation. This is seen to correspond with the dicrotic notch of the carotid tracing. Immediately following the completion of systole there is a small, rapid rise of pressure from 3 to 4.

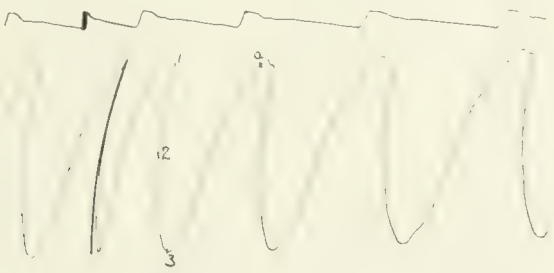

Fig. 10.—Simultaneous tracing of carotid pressure (upper curve) and of volume curve of normal ventricle (lower curve). The heart rate is increased to the optimum rate. The period of diastasis is abolished and the auricular systole (a) follows immediately the ventricular relaxation. The filling is complete. Systolic output, 12 c.c.

Henderson believes that this is due to the rapid entrance of blood into the coronary vessels after they are released from the compression of the contracted ventricles. For an instant after this sudden rise of pressure there is a delay from 4 to 5, followed by a large upstroke *which is almost as rapid as the systolic discharge.* The tracing shows the ventricles have filled at 6 in .43 of a second, early in diastole, and they remain in this quiescent state until the onset of the following auricular systole. At 7 the auricle contracts, and it is seen that it ejects only a fraction of a cubic centimeter of blood into the already filled ventricle.

RELATION OF HEART RATE TO THE AMOUNT OF SYSTOLIC OUTPUT.

While the preceding tracing may be taken as typical of the heart beating at a normal rate, Figure 10 shows the changes which occur when the rate of the heart beat is increased. Tracing No. 25 shows, after

vagal stimulation, the effect of a slowing of the heart. It will be seen that at the higher rate the rate of discharge or refilling has not appreciably varied. The change has involved only a shortening, and in this case abolition of the period of quiescence. On the other hand, after vagal stimulation, the duration of systole and relaxation have remained the same, but slowing has been affected by lengthening the interval of rest. It is evident that an increase of rate up to the point which abolishes the period of quiescence increases the amount of blood thrown out into the aorta, per unit of time, and, other things being equal, it will increase the work done by the heart and also the mean pressure in the arterial system.

If, however, the heart be made to beat at a still higher rate (Fig. 11), the relaxation curve is encroached on by the following systole and, complete filling being prevented, it will involve a diminution in the amount of blood discharged at that systole. The work done by the heart in such

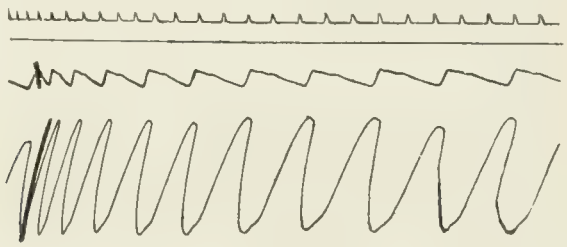

Fig. 11.—Upper curve, carotid pressure. Lower curve, volume curve of ventricle. This shows effect of a very fast heart rate. Not only is there no period of diastasis, but the ventricular filling is interfered with by the following systole. The output at each contraction is diminished. Systolic discharge, 8 c.c. Time in fifths of a second.

a case is not increased, for, although the rate is greater, the amount thrown out at each systole is less, and, therefore, the output per unit of time does not vary.

The conclusions, then, which are to be drawn from the volume curves of the ventricles are:

First.—That the part played by the systole of the auricles is of little importance in the filling of the ventricles. They act more as elastic reservoirs than as muscular force pumps. The force which fills the ventricle is acquired from the potential energy stored in the walls of the auricles from their distension by the venous pressure. The ventricles are not filled by the contraction of the auricles, for they are already full before the onset of auricular systole. Henderson thinks that the wave of increased pressure sent into the ventricles by the auricular systole has as its function only the closure of the auriculoventricular valves, which have previously been floated into position by the inflow during diastole.

Second.—That the rapidity of ventricular relaxation is independent of the rate of the heart, and is an unalterable characteristic for each heart.

Third.—That the cardiac cycle is not diaphasic but triphasic, and "consists of systole, the period of contraction and discharge, diastole the period of relaxation and filling; diastasis, the period of rest."

EFFECT OF VOLUME CURVES OF VENTRICLES WHEN AORTIC VALVES ARE DAMAGED.

The most satisfactory method of comparing the volume curves before and after insufficiency is to trace the normal on transparent paper and lay this over the abnormal. It is necessary for this purpose that the heart rate be the same in the two tracings and the rate of rotation of the drum

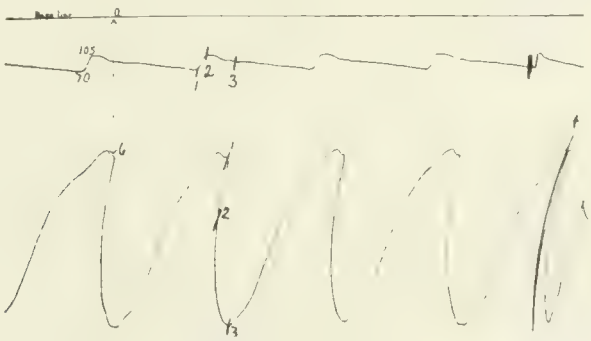

Fig. 12.—Carotid and plethysmographic curves taken immediately before the production of insufficiency. Systolic pressure, 105; diastolic pressure, 70; systolic output, 12.8 cc. The line a-b represents the ventricular tonus.

constant. Figures 12 and 13 are the actual tracings taken before and after the production of insufficiency.

When the tracings are superimposed (Fig. 14) it will be seen, contrary to expectation, that the rapidity of ventricular output is slower in aortic insufficiency than it is normally. This is proved by the fact that the apex of the curve is reached in the normal in .18 second, while in the abnormal it occupies an interval of .22 second.

The amount of ventricular output differs in the two by only ½ c.c. of blood. This is in direct contrast to the views at present held regarding regurgitation. It is thought that the amount of blood which returns to the ventricle when added to that which normally enters from the auricle is sufficient to cause a dilatation of the ventricles. Even with the most extensive damage to the valves, the increased systolic output did not exceed the normal by more than 1 c.c. of blood.

The upstroke, that part of the tracing which represents the cardiac filling, shows that the ventricle fills somewhat faster in the abnormal condition. Its acceleration, however, involves only the commencement of diastole proper, as is demonstrated by the more gradual ascent of the first part of the uprise. After the ventricles have filled to about one-fifth of their capacity, the rate of filling becomes the same, the remaining part of the uprise being gradual. When the heart remains the same, the time lost by the longer systole is compensated for by this increased rate of filling in early diastole.

If, now, the distance between the diastolic positions of the curves and the base line be compared in the two tracings, an indication will be

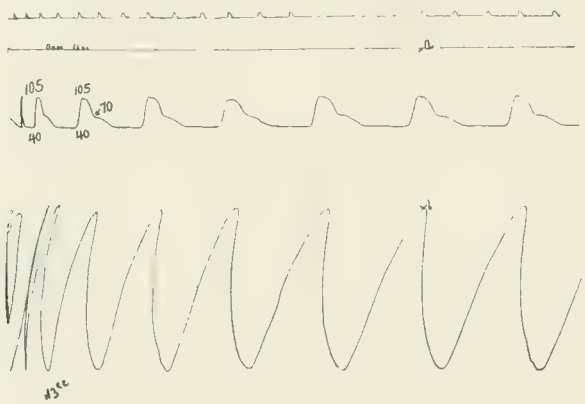

Fig. 13.—Carotid pressure and ventricular volume curve after the production of aortic insufficiency. Systolic pressure, 105; diastolic pressure, 40; systolic output, 13 c.c. The line a-b represents the ventricular tonus. Compare with tracing No. 12, in which it is shorter. This indicates that the ventricle is less distended. Ventricular tone and distension vary inversely with one another.

given of the relative distension in the two conditions. The "base" in this instance being situated above the tracing, it is, of course, evident that the shorter this distance the greater the ventricular distension, and *vice versa*. On the other hand, the further the systolic portions of the curves are from the base line the more completely do the ventricles empty themselves.

It must be recalled that the systolic discharge volume of the normal heart is not necessarily an indication of the amount of ventricular distension or of the actual amount of blood which the ventricle contains. As Henderson[17] has shown, it is about 60 per cent. of the total volume difference between extreme distension as would follow a prolonged vagus

17. Loc. cit., p. 365.

stimulation and extreme contraction, as exhibited in hearts which have stopped beating in systole.

A constant systolic discharge may be obtained in one of three ways. (1) It may occur with the normal amount of relaxation and the normal degree of ventricular contraction. (2) With an increased relaxation and less complete ventricular contraction, the residual blood being increased. (3) With a diminished relaxation and a more complete systole, in which case the residual blood is diminished.

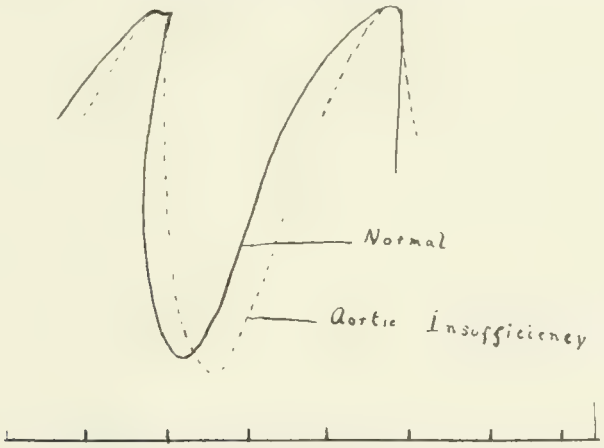

Fig. 14.—Superimposed tracing of the normal ventricle and that of the ventricle after the production of aortic insufficiency. The rate of systolic discharge is slower in abnormal state.

These different states of the ventricle are represented diagrammatically in Figure 15. As to which of these three conditions will obtain will depend entirely on the ventricular tonus. A comparison of this distance in the two tracings (12 and 13) reveals the surprising fact that the production of aortic insufficiency causes the ventricle to contract in Condition 3, viz.: with a diminished relaxation and more complete systole. The amount of residual blood which is known to exist normally is diminished, and, while the ventricular filling is slightly greater, the ventricle at the end of diastole is less distended. This is also shown in Figure 18.

It is impossible, in view of these facts, to accept the statement of Johannsen and Tigerstedt,[18] that in experimental aortic insufficiency the ventricle does not empty itself so completely. This statement was based chiefly on the theoretic grounds that when the ventricular cavity is dilated the blood is less completely expelled during systole. But it has

18. Skand. Arch. f. Physiol., i, 331.

been shown above that the ventricle is less distended after the simple production of aortic insufficiency, and this can only result from an increased ventricular tonus. It will be shown later that if the tone is diminished the ventricle dilates and the amount of residual blood becomes increased. The comparison of the tracings, however, furnishes important information on the quantity of blood which regurgitates. In the animal from which these tracings were taken the posterior cusp was completely divided by MacCallum's valvulotome, and a greater degree of insufficiency thus produced than can probably occur in man as a

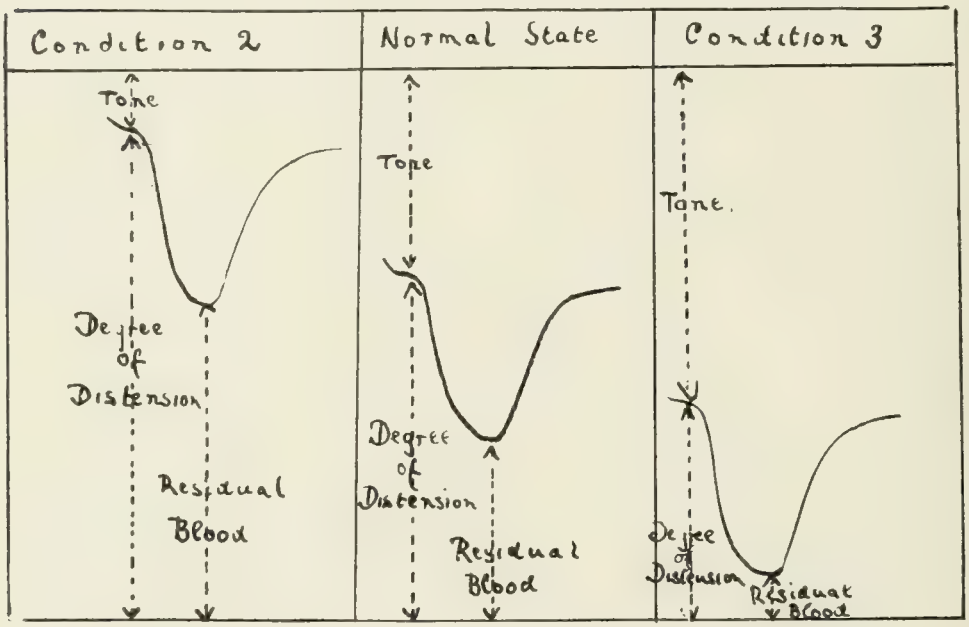

Fig. 15.—Diagram to illustrate the different conditions under which the ventricle with intact valves may contract. The curves represent a plethysmogram, indicating the same amount of systolic discharge in the three conditions. The length of the interrupted lines indicates the degree of tonus, the degree of distension and the amount of residual blood, respectively. In Condition 2 there is an increased relaxation and an increased amount of residual blood, but a diminution of the degree of tonus. In Condition 3 the tonus is increased, while the degree of distension and the amount of residual blood are diminished. Tonus varies inversely with distension and the amount of residual blood.

result of disease. As stated above, the systolic output in the two cases, at the same pulse rate, differed only by ½ c.c. of blood. There was no diminution in the amount of blood delivered by the auricle, as was evidenced by the fact that there was no dilatation of its cavity.

The facts admit of but one interpretation, viz.: that after an extensive valvular lesion the actual amount of blood which regurgitates is fractional in quantity as compared with that which enters naturally from the auricle.

It may, then, be asked why the loss of so small a quantity of blood should give rise to the various phenomena associated with this lesion. The point will at once become clear when one understands that the essential change is a loss of pressure rather than a transference of blood from the aorta to the ventricle. It must, of course, be admitted that some blood must regurgitate, but the conditions under which the regurgitation occurs, are such that it becomes of the smallest possible amount. The aorta and ventricle being in direct communication, the pressures in the two chambers will tend to become equalized, and the curves of intraventricular and arterial pressures will show that this does occur. But a transference of pressure does not necessarily presuppose a transference of blood, just as a rise of pressure in the radial artery during the passage of the pulse wave is not due to a corresponding increase in the amount of the radial blood stream.

The tendency toward regurgitation is lessened in the first place by the low pressure which will be shown to obtain in the aorta immediately after the completion of systole. This systolic end pressure or that which is present at the termination of the systolic plateau will be shown, also, to be very different from that which is produced at the summit of the primary wave, and the relation of the two is an indication of the rapidity of capillary flow. It is entirely distinct, although it does not differ, on an average, by more than 15 mm. mercury from the pressure in the aorta at the end of diastole. The difference in pressure between the systolic end pressure and that at the end of diastole is accounted for partly by the loss due to regurgitation and partly by the capillary escape. Under no circumstances, then, can this fall of pressure due to regurgitation exceed or even equal this difference.

But another factor contributes to the prevention of a large amount of regurgitation of blood, viz.: the rapidity of ventricular filling. At the moment of ventricular relaxation, the pressure in the left ventricle is negative, and, as a result, the aortic and auricular blood are rapidly forced toward the ventricle. But since, as has been shown already, in the physiologic condition the ventricle receives venous blood only during the early part of diastole, the outflow from the auricle must take place with extreme rapidity. In the pathologic condition, while the difference between the pressures in the left auricle and the aorta is still great, and would increase the rapidity of stream from the latter, the great differ-

ence in size between the two openings through which the blood enters will render the amount of blood delivered from the aorta insignificant as compared with that which comes from the auricle. The ventricles will have filled, therefore, before an appreciable quantity has returned from the aorta. And since the volume curves show that the ventricular tone is greater, immediately the filling is completed, the ventricles are able to withstand the relatively low pressure which is transmitted from the aorta without becoming further distended. When the intraventricular pressure curves are presented, it will be seen that at the end of ventricular repletion the pressure has already reached that which obtains in the aorta, and during the period of diastasis there is no further increase of intraventricular pressure.

The change in form which results in the volume curve as a consequence of increased tension at once suggests an analogy with the corresponding effect of tension in the contraction of a skeletal muscle. The

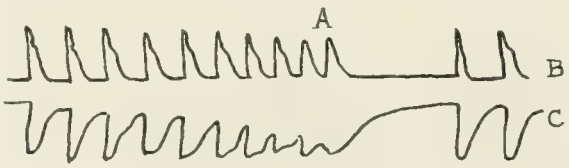

Fig. 16.—Simultaneous isometric and isotonic contractions of the frog's gastrocnemius.

similarity, which was first referred to by Francois Franck[19] between the volume curve and the isotonic muscular contraction and between the intraventricular pressure curve and an isometric contraction in the normal heart, was subjected to experimental test by Henderson.[20] By means of an apparatus called a work adder he was able to cause a skeletal muscle (a frog's gastrocnemius) to record simultaneously an isometric and an isotonic curve. In an isometric contraction the muscle is made to contract against a resistance which it is unable to overcome. The resistance commonly employed is a strong spring, and the small excursion induced is greatly magnified by the use of levers. The shortening which results in the muscle being negligible, the curve indicates the changes in tension which the muscle undergoes. An isotonic contraction, on the other hand, is one in which the muscle is, or is not, loaded with a weight which it is able to lift, and the natural shortening is not impeded. The isometric curve is distinguished from the isotonic by the more rapid uprise, indicating that the greatest tension is reached much sooner than

19. Trav. du lab., de Marey, 1877, iii, 321.
20. Loc. cit., p. 357.

the greatest shortening, and by an apex which is flat topped instead of rounded. Henderson's simultaneous isometric and isotonic curves (Fig. 16) show in a striking manner the close resemblance which they bear, respectively, to the pressure and volume curves of the normal ventricle.

As a skeletal muscle is influenced in the form and strength of its contraction by changes in the tension which precede or accompany its contraction, so also is the heart when increased tension is thrown on it, as a consequence of abnormal states. Starling[21] holds that in the normal state the ventricle contracts isotonically, since after overcoming the aortic pressure the muscle fibers can shorten without further hindrance, while in aortic stenosis the ventricle meets with resistance during the whole period of its systole, and, therefore, approximates an isometric contraction. In aortic insufficiency, however, we have a condition in which the increased tension is exerted before the onset of the ventricular contraction and is comparable to the "loaded" isotonic curve. The normal volume curve is similar to the "after-loaded muscular contraction," that is to say,

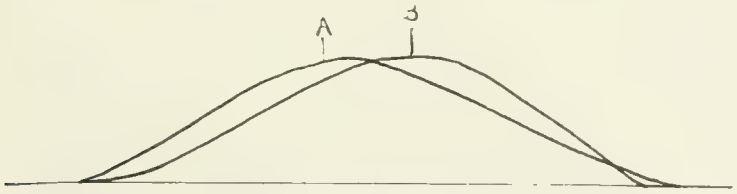

Fig. 17.—A. After-loaded contraction. B. Loaded contraction.

the tension to which the muscle is subjected is that of the load, and it begins to act only after the muscle has already contracted. The ventricles are subjected to no tension before contracting, and, after reaching a certain degree of contraction, the tension remains constant until the end of systole. It is different, however, when the aortic values are incompetent. Here a considerable tension exists in the ventricular walls as a consequence of the transmission of pressure from the aorta. The condition is the same as that which exists in a loaded muscle preparation, tension is applied to the muscle before it contracts. A comparison of the two volume curves at once shows their resemblance to an after-loaded and a loaded muscle, respectively.

The inversion of the volume curve will render the resemblance still more striking. The above curve (Fig. 17) is based on the work of von Kries[22] and shows the effect of applying tension to a muscle prepara-

21. London Lancet, 1897, i, 570.
22. Arch. f. Physiol., Leipz., 1880, p. 370.

tion before contraction. The uprise is more gradual, showing that the rate of contraction is diminished, and the summit of the loaded curve follows that of the after-loaded muscle. It will be recalled that the volume curve of the ventricle in aortic insufficiency differs from the normal in exactly the same respects. It was shown that the rate of ventricular output is slower, and the time taken to effect complete systole delayed.

But the comparison may be extended further. The ventricular contraction of the normal heart is analogous to that in a muscle which contracts and at the summit of its contraction is relieved of its load and allowed to relax without any extending force. The heart in aortic insufficiency, however, is comparable to the muscle which is subjected to ten-

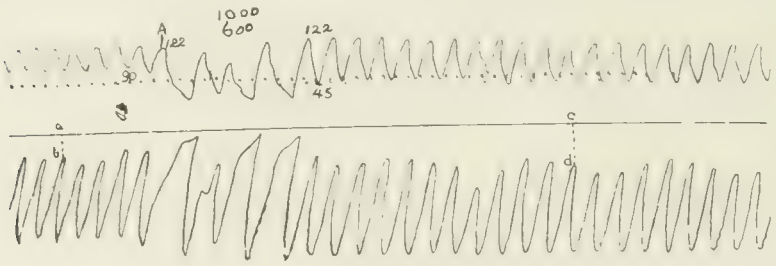

Fig. 18.—Carotid pressure and ventricular volume curve to show the effect of the production of aortic insufficiency. (a) Equals insufficiency produced. The systolic pressure remains the same, 122 mm. of Hg., but the diastolic pressure falls from 90 mm. Hg. to 45 mm. Hg. The volume curve shows that for four beats after the production of the lesion the ventricle becomes considerably dilated, and at this moment regurgitation does probably occur. After a lapse of about two seconds, however, the ventricle recovers itself and the distension becomes less afterward than before. The line c-d is longer than a-b, equals increase in the ventricular tone. The ventricle also empties itself more completely. The apex of the volume curve is further from the base line.

sion during the phases of contraction, elongation and rest. The effect of tension so applied is to increase the rapidity of elongation, and to this action we may attribute the more rapid uprise of its volume curve. The conclusion arrived at by Schenck[23] in relation to the effect of tension on the contraction of skeletal muscle may with equal force be applied to the ventricle: "Tension protracts contraction and hastens relaxation."

EFFECT ON BLOOD PRESSURE OF RUPTURE OF THE AORTIC VALVES.

Cohnheim,[9] in his classical experiments, found that, although the valves are ruptured and no longer able to effect closure during diastole, "the mean arterial pressure remains at precisely the same level." Rosenbach[12] repeated his experiments and obtained the same results. Since then

23. Arch. f. d. ges. Physiol., Bonn, 1894, lvii, 606.

the investigation has been undertaken by numerous other observers, but their experiments do not, in every case, agree with those of Cohnheim and Rosenbach. While MacCallum[16] found that the blood pressure remains remarkably high, Kornfeld[11] noticed that it may either be increased or diminished.

These experimenters, without exception, used the ordinary mercury manometer attached to the carotid artery. As is well known, this instrument does not follow promptly the quick changes of pressure which occur between systole and diastole, and the limited excursion gives only an approximate reading of the mean blood pressure; nor, on account of its relatively sluggish movement, can either the systolic or diastolic pressures be accurately measured. The use of the Huerthle manometer, along with the maximal and minimal valves, gives a ready means whereby both systolic and diastolic pressures can not only be measured accurately, but also recorded.

The following table gives the result of the production of aortic insufficiency on the maximal and minimal blood pressures in ten experiments:

Expt.	Before.		After insufficiency.			
No.	Sys.	Dias.	Sys.	Dias.	Lesion.	Result.
1	125	90	125	50	Post. cusp.	Dog survived shock of lesion.
2	126	80	90	20	Int. cusp.	Dog died.
3	140	120	140	30	Post. cusp large.	Dog survived.
4	115	80	115	28	Ext. cusp.	Dog survived.
5	105	70	75	35	Post. cusp.	Dog died.
6	170	155	100	40	Post. cusp.	Dog died.
7	100	70	100	45	Post. cusp.	Dog survived.
8	155	120	160	80	Ext. cusp.	Dog survived.
9	150	72	150	50	Post. cusp.	Dog survived.
10	120	90	85	10	Post. cusp.	Dog died.

It will be seen that in none is the systolic pressure increased after the valves are rendered incompetent. In those cases in which the animals survived the shock of the lesion, the *systolic pressure remained at exactly the same level.* The diastolic pressure invariably undergoes a diminution which was found not to depend entirely on the amount of damage done to the valves. While the systolic pressure is not affected by the lesion, the mean pressure falls, since, as shown by Dawson,[24] it is nearer and follows the diastolic pressure much more closely than the systolic. In all the experiments, therefore, the mean blood pressure fell. It is to be noted that in those animals which succumbed after the production of the insufficiency the systolic pressure also underwent a marked diminution. This merely indicated that the heart was failing and unable to eject the previous quantity of blood. The ventricles under these cir-

24. Ref. Erlanger and Hooker, Johns Hopkins Hosp. Rep., 1904, xii, 150.

cumstances gradually dilated and stopped beating in diastole after the lapse of about ten minutes. And while the fall of systolic pressure resulted from a lessened output the maintenance of the systolic pressure showed that the amount of systolic output in the non-hypertrophied and non-dilated heart did not vary. This was also shown by the volume curves of the ventricles after damage to the aortic valves.

In the meantime it is to be emphasized that the mean blood pressure falls considerably, and this fall is proportional to the fall in the diastolic pressure, the systolic pressure remaining the same as before.

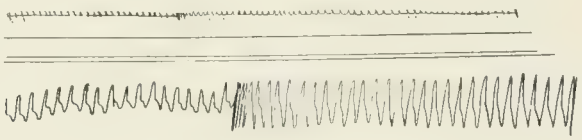

Fig. 19.—Carotid tracing to show the effect of rupture of the aortic valves. Systolic pressure 150 mm. Hg. before and after the lesion. Diastolic pressure falls from 70 to 50 mm. Hg.

It was frequently observed in the earlier experiments that when the valvulotome failed to enter the sinus of Valsalva, but passed directly into the ventricle without damaging a valve, the curve assumed the form seen in undoubted insufficiency. There was an immediate fall in blood pressure, with a great increase in the pulse pressure. Indeed, on two separate occasions the collapsing character of the pulse which resulted was so marked that it was assumed that a valve was cut, and the experiment was proceeded with without again introducing the instrument. When,

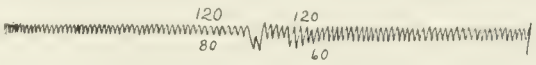

Fig. 20.—Carotid tracing showing the fall in diastolic pressure from irritation of the posterior wall of the ventricle by the valvulotome. There was no insufficiency produced. Systolic pressure before and after, 120 mm. Hg.; diastolic pressure before, 80 mm. Hg.; diastolic pressure after, 60 mm. Hg.; slow drum.

however, the heart was examined postmortem, one was astonished to find that the valves were absolutely intact. In a third experiment it was thought that an insufficiency was obtained, but after the lapse of about an hour the collapsing character of the pulse disappeared and, in view of the previous experience, it was suspected that the instrument had merely entered the ventricle without damaging the valves. It was again introduced and the external cusp torn, which was found on autopsy to be the only valve damaged. The tracings of these experiments are shown in Figures 20 and 21.

In seeking for an explanation of this phenomenon one was at first inclined to believe that it was due to the presence of the instrument in the mouth of the aorta which prevented closure of the valves. This, however, could not have been the cause, since the collapse persisted after the withdrawal of the instrument.

It seems not at all unlikely that the rubbing of the point of the instrument on the posterior wall of the ventricle mechanically stimulated the endings of the depressor nerve and thus brought about the immediate fall in blood pressure. This hypothesis seems justifiable, in view of the fact that Köster and Tschermak[25] showed anatomically that the nerve ends partly in the wall of the ventricle and partly in the aorta beyond its mouth. Whatever the explanation is, the observation has an important bearing on the question of the collapsing pulse. It proves that this type of pulse is not peculiar to aortic insufficiency, but can be obtained in any condition in which, with a persistence of ventricular activity, there is a fall in the diastolic blood pressure.

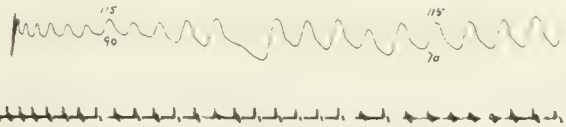

Fig. 21.—Carotid tracing to show also the fall in diastolic pressure which results from passage of the valvulotome into the ventricle without damaging a valve. Diastolic pressure fell from 90 to 70 mm. Hg. No change in systolic pressure.

COMPARISON OF THE NORMAL PULSE WITH THAT OBTAINED AFTER PRODUCTION OF AORTIC INSUFFICIENCY.

Huerthle[4] has shown, and the plethysmographic tracing confirms it, that the period which elapses between the appearance of the primary and the dicrotic wave is an accurate measure of the outflow from the heart during systole. Of course, it is evident that it is not synchronous with the commencement and termination of systole, since a fraction of a second elapses before the ventricle gathers sufficient strength to open the semilunar valves, and a definite interval also elapses after the end of systole before the appearance of the dicrotic waves. Huerthle found, however, that these intervals are of the same length; therefore, all changes occurring between those points are included in the systolic phase of the pulse curve.

Since the abnormal condition induced by the rupture of the aortic valve does not affect the mechanism of the production of the systolic

25. Arch. f. d. ges. Physiol., Bonn, 1902, xciv, 24.

portion of the pulse curve, that phase can be compared, point by point, in the two pulses. While in the pulse of aortic insufficiency the diastolic portion is the product of an abnormal mechanism, the systolic in both is affected physiologically.

The Amplitude of the Ascending Limb of the Pulse Wave.—The production of aortic insufficiency invariably increases the pulse pressure. The following table shows the increase which took place in six experiments:

Expt.	Before insufficiency.			After insufficiency.		
No.	Sys.	Dias.	Pulse pressure.	Sys.	Dias.	Pulse pressure.
1	125	90	35	125	50	75
2	140	120	20	140	30	110
3	115	80	35	115	28	87
4	100	70	30	100	45	55
5	155	120	35	160	80	80
6	150	72	78	150	50	100

According to Marey,[26] it was first demonstrated by Hales, and afterward by Bernard, that when the blood pressure falls, the amplitude of the pulse is increased. Marey himself confirmed their observations, and more recently the investigation has been revised by Huerthle[27] with improved methods. He showed that the fall of blood pressure resulting from stimulation of the depressor nerve is accompanied by an increase of the pulse pressure, and conversely that the rise of blood pressure from splanchnic stimulation diminishes the pulse pressure.

Granted, then, a constant systolic output, vasodilation will increase the pulse pressure by lowering, while vasocontraction will diminish it by raising the diastolic blood pressure.

But the pulse pressure is materially influenced by the amount of blood ejected at each ventricular systole and by the relative capacity of the arterial tree. Different amounts of blood, thrown into an arterial system whose capacity does not vary, will produce differences in pulse pressure which will be greater the larger the systolic output. The difference will be affected by an increase of the maximum pressure rather than by a lowering of the mean or diastolic pressure.

If, then, after the production of aortic insufficiency increase of the pulse pressure be accompanied by an increased systolic pressure, the diastolic remaining the same, it must have resulted from an increased systolic output. If the diastolic pressure is lowered and the systolic pressure remains as before, there must have been an attendant vasodila-

26. La Circulation du Sang., p. 269.
27. Pflueger's Arch., 1888, xxxiv, 393.

tion. If, on the other hand, the increased pulse pressure is the result of a lowering of the diastolic and an increase of the systolic pressure, it must have been caused by a true regurgitation. The regurgitated blood will have been added to the normal systolic output, thus raising the maximum pressure, while the diastolic pressure will have been lowered by the loss of the same amount.

The actual conditions which obtain in experimental aortic insufficiency have already been shown (page 123). It was shown that when the animal survives the production of the lesion, the systolic pressure remains at exactly the same level, whereas the diastolic pressure falls in a very marked manner. The pulse pressure has been increased because of this fall, and, as above stated, it can only have resulted from peripheral dilatation.

The Systolic Plateau.—That portion of the pulse curve which extends from the point of maximum pressure to the commencement of the dicrotic notch has been termed by Marey the systolic plateau. This plateau may be horizontal, ascending or, as in the normal pulse, descending.

Fig. 22.—After Marey.

When it is horizontal the inflow of blood is exactly equal to the systolic escape from the capillaries. When it ascends, as in the anacrotic pulse, the escape is less than that received into the arterial system, and the pressure continues to rise. When it descends the indication is that the systolic escape by the capillaries is greater than the systolic influx. It naturally follows that the steeper the declivity of the systolic plateau, the greater is the excess of the systolic escape over the systolic inflow. Such, for instance, can always be seen to take place in the normal pulse when the capillary flow is accelerated from dilatation of the peripheral arterioles by the administration of nitrate of amyl.

The comparison of the normal pulse with that obtained after the production of aortic insufficiency shows the much greater systolic fall of the latter. Indeed, the main fall of pressure is composed of this declivity, for the amount of fall which is purely diastolic, viz., from the dicrotic notch to the abscissa, is almost negligible, as compared to that which occurs in systole.

It must be conceded, then, that from the form of the pulse curve alone we have evidence that the essential feature of the collapsing pulse lies in the systolic phase of the cardiac cycle. The pulse differs in no way from that in which, with the maintenance of ventricular activity, there is a relaxation of the peripheral resistance.

EFFECT OF CHANGES IN HEART RATE IN AORTIC INSUFFICIENCY.

From the examination of the volume curves of the normal heart it was shown that an increase of rate up to a certain limit increased the amount of systolic output per unit of time. The action is due to the shortening of the period of diastasis, which allows of an increase of heart rate, without interfering with the ventricular filling. Erlanger[28] and Hooker observed that an increase in the quantity of blood thrown out in a given time will increase the mean and therefore the diastolic pressure in the arterial system. In aortic insufficiency an increase in the diastolic blood pressure must increase the pressure which is transmitted to the ventricular walls during diastole. Any increase of rate, however, beyond that which abolishes the period of diastasis occurs at the expense of diastole, in Henderson's sense (i. e., time of filling), for each succeeding systole will take place before the normal relaxation of the ventricle is completed. The blood thrown out during systole must, then, be diminished, and while the heart beats more rapidly, the output in a given time does not vary. The diastolic pressure will, therefore, undergo no further augmentation.

Disregarding for the time being the possible influence which a lengthening of the period of diastole and diastasis may have on regurgitation, it is evident that in so far as aortic pressure is affected by changes in rate a slowing of the pulse within normal limits will not affect the pressure which can be transmitted to the ventricle, whereas an undue lengthening will lower it. Regarded in this light, an unusually slow heart rate is advantageous in aortic insufficiency.

This effect of rate, however, becomes secondary to that which it has on regurgitation and transmission of pressure. It is usually taught that a lengthening of the period of diastole is disadvantageous in that it increases the leak into the ventricle and causes it to dilate. This is clearly based on the conception that an "appreciable" quantity of blood returns to the ventricle. It has been shown in the plethysmographic records that the volume of the blood which regurgitates in experimental insufficiency is negligible, and that the phenomena associated with the

28. Johns Hopkins Hosp. Rep., 1904, xii, 160.

condition are due to the attendant transmission of pressure. An estimation, then, of the rate at which this pressure is transmitted will give the desired information as to whether a lengthening of the period of diastole and diastasis is harmful or advantageous. For, clearly, if the pressure in the ventricle equals that in the aorta at the end of ventricular relaxation, it is immaterial how long the period of diastasis may be, since it will involve no further increase of the intraventricular pressure. If the pressure, on the other hand, is transmitted slowly from the aorta to the ventricle; that is, if the intraventricular pressure rises gradually during the whole period of diastole and diastasis and equals the aortic pressure just before the following systole, then a lengthening of the period of diastasis will have a harmful effect.

In order to determine which of these conditions holds in aortic insufficiency the curve of intraventricular pressure was recorded in three experiments.

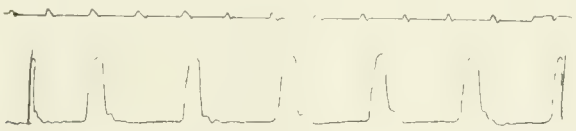

Fig. 23.—Intraventricular pressure tracing from the normal ventricle. Contrast with tracing No. 24.

Figure 24 is the intraventricular pressure curve after the posterior aortic cusp was divided. It shows a somewhat oblique upstroke, which corresponds closely to the protracted volume curve of systolic discharge. The systolic plateau is rounded and merges insensibly into the diastolic downfall. The fall in pressure is at first rapid, but it becomes more gradual as it approaches the abscissa. This latter point is of great importance, for it stands in marked contrast with the abrupt and uniform fall in pressure which is seen in the intraventricular pressure curve of the normal heart, as in Figure 23.

It will be recalled that the plethysmographic records showed that the effect of aortic insufficiency was to increase the tonus of the ventricle, and, as a consequence, its distension during diastole was less than in the normal heart. It was shown also that the increased rapidity of filling took place only during the first fifth ventricular relaxation. This of itself would indicate that at the end of this period, viz., the first fifth of relaxation, a certain amount of aortic pressure had already been transmitted to the ventricle, and its further relaxation was effected with an increasing tension on its walls. As is well known, the pressure in

the normal ventricle falls below atmospheric pressure immediately after the ventricle begins to relax, as a consequence of the suction action exerted by its walls. If, as in aortic insufficiency, a positive pressure is being transmitted at the same time from the aorta, it should follow that this fall in pressure will become less rapid, and the downstroke of the intraventricular curve more inclined. That such is really the case, tracing No. 24 proves.

On the one hand, the relaxation of the ventricle tends to produce a diminution of the pressure within it, while, on the other hand, the free communication with the aorta will permit of the transmission of positive pressure. The excess (algebraically) of the negative over the positive will occasion a fall of the intraventricular pressure curve, which will be slow or rapid according as the excess is small or great. In other words, if the aortic diastolic pressure is high, and the communication between it and the ventricle large, the fall in pressure in the latter, during its relaxation, will be more gradual than if the leak were small or absent. Further, it is evident that the fall will be more rapid at the begin-

Fig. 24.—Intraventricular pressure curve after production of aortic insufficiency. The upstroke a-b is more gradual, as is also the fall in pressure b-c. The line c-d is horizontal, showing that the intraventricular pressure does not rise during the period of diastasis. The figures represent the pressure in mm. of Hg. at different points of the curve.

ning of the process of equalization than near its termination, since then the negative relaxation pressure in the ventricle is greatest. The rate of fall, therefore, is seen to be more gradual as the downstroke reaches the abscissa, for the negative pressure is being gradually neutralized by the positive.

The most striking feature, however, of the curve of intraventricular pressure lies in the fact that the downstroke does not reach the abscissa at any stage of the diastolic phase. Following the gradual fall of pressure which accompanies the completion of ventricular relaxation, the lever traces a line which runs parallel to the abscissa, and in this instance indicates a pressure of 40 mm. Hg. But the rapidity with which the aortic pressure is transmitted to the ventricle varies directly with the size of the communication. It follows, therefore, that when the insufficiency is extensive, the pressures in the aorta and ventricle become equalized during the period of relaxation, and there is no further transmission in the phase of ventricular diastasis. This proves conclusively

that, under such circumstances, if the tonus of the ventricle is maintained a slowing of the heart rate can not have a harmful influence in aortic insufficiency.

It is possible, however, in those cases in which the opening between the aorta and ventricle is small that the delay in the transmission of aortic pressure which results may cause the pressure in the ventricle to rise during the whole period of diastole. The smallness of the communication probably accounts for the rise of diastolic pressure seen in the tracings of Marey.[29]

He produced an aortic insufficiency in the horse by the passage of a cardiac sound which merely punctured an aortic cusp. An insufficiency thus produced is much smaller than that which follows section of the cusp. Further, it was noticed in the present series of experiments that an opening in a valve produced by the cardiac sound becomes blocked

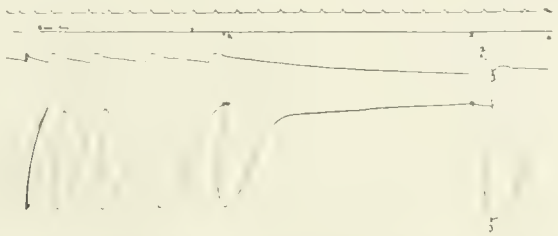

Fig. 25.—Carotid and ventricular volume tracings from the normal heart, showing the effect of vagal stimulation. The difference between the lines a-b and x-y represents the distension of the ventricle due to loss of tone = 1 c.c. of blood. Stimulation of the nerve slows the heart rate by prolonging the period of diastasis. The rapidity of ventricular filling is not affected. The marks on the base line indicate the period of stimulation.

rapidly by the formation of a fibrin clot. In one such experiment a clot had formed in an hour, and many of the features of this condition became distinctly less marked.

A gradual rise of pressure, then, is possible when the communication is small, and only under such circumstances can a slowing of the pulse rate, *per se*, be said to have a harmful influence on the ventricle. A similar conclusion as to the effect of rate is arrived at from the results obtained by stimulation of the peripheral end of the vagus nerve.

EFFECT OF VAGUS STIMULATION.

The effect of the stimulation of this nerve has purposely been omitted from the discussion of the relation of heart rate to aortic in-

29. Loc cit., 674.

sufficiency, since stimulation of the vagus gives rise to two (among several) distinct physiologic changes in the ventricle.

As is well known, when the peripheral end of the vagus is stimulated, in addition to slowing of the ventricular contraction, it diminishes ventricular tone. The two effects can not be disassociated, and, while at first we would appear to have a ready means of studying the effect of rate on regurgitation, we are immediately confronted with the difficulty that arises as a result of the diminution of tone, simultaneously induced.

When the vagus is stimulated the volume curve of the normal heart shows that the ventricle becomes gradually distended (Fig. 25). This follows from the fact that the auricular pressure, although small, is sufficient to overcome the diminished tone of the ventricular walls.

If after aortic insufficiency has been produced the nerve is stimulated with the same strength of current and for the same length of time, any distension which may take place beyond that which occurs normally

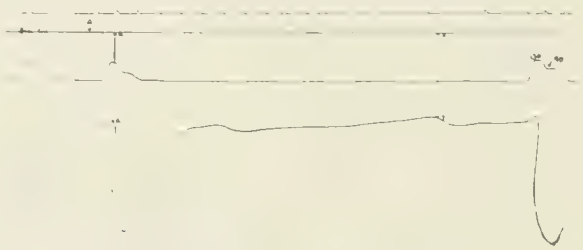

Fig. 26.—Carotid and ventricular volume tracings after the production of aortic insufficiency. The vagus nerve was stimulated at A and the loss of tone causes the ventricle to dilate. The amount of distension produced (difference between a-b and x-y) is the same as in the normal heart—1 c.c. in each. The slowing of the heart rate, therefore, can not allow of regurgitation of blood.

under vagus stimulation will result from regurgitation. In this manner only is it possible to draw any accurate conclusions as to the effect produced by slowing the heart rate experimentally by vagus stimulation.

In order to confirm the findings obtained by the records of the intraventricular pressure curves, two such tracings are reproduced. In the normal, Figure 25, the effect is seen to involve only the period of diastasis. The vagus standstill allows the completion of diastole, which is completed in the usual time, in this case .272 of a second. The line of prolonged diastasis inclines gradually upward, and indicates a distension of the ventricle from loss of tone.

Practically the same thing is seen to occur in tracing No. 26, where the aortic valves have been damaged and the distension which results

is no greater than that which occurs in the normal heart, 1 c.c. of blood in each.

Before stimulation the tone of the heart whose valves were damaged was greater than that of the normal, in consequence of the mechanical stimulation of increased intraventricular pressure. During stimulation the tone is reduced in both in the same degree, and a correspondingly equal distension is produced in the two states.

It is interesting to note that even after vagus stimulation the tone of the ventricle, when the aortic valves are damaged, as measured by the distance of the volume curve just before systole from the base line, is equal to that which obtains normally in the heart with intact valves.

This experiment has a twofold bearing. Taken in conjunction with the intraventricular pressure curves, it proves beyond doubt the relative unimportance of heart rate, *per se,* while, on the other hand, it emphasizes the important rôle which the ventricular tonus plays in the prevention of extreme regurgitation.

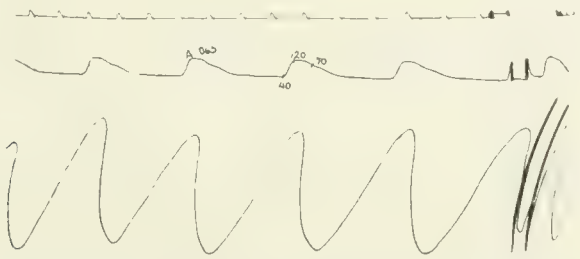

Fig. 27.—Carotid and ventricular volume curve in aortic insufficiency before compression of the abdominal aorta. A, summit of the primary wave. It is reached in .065 of a second after the commencement of systole. Systolic pressure, 120 mm. of Hg.; pressure at beginning of diastole, 70 mm. of Hg.; pressure at the end of diastole, 40 mm. of Hg.; systolic output, 12 c.c. (Compare with tracing No. 28.)

EFFECT OF INCREASING PERIPHERAL RESISTANCE.

The examination of the pulse of aortic insufficiency, and the similarity between the action of a true rupture of the aortic valves and an irritation of the ventricular wall in lowering blood pressure, have suggested the importance of a vaso-dilatation as the important factor in the causation of the collapsing pulse. It becomes necessary, then, to test experimentally the effect of changes in the peripheral resistance.

There are three methods by which it is possible to obtain varying degrees of increased resistance: (1) By stimulation of the splanchnic nerves; (2) by the injection of adrenalin; (3) by compressing the abdominal aorta.

While the first method in general is the most satisfactory, it was found that under the circumstances in which the records were obtained in this research it was impracticable. The dissection necessary to stimulate these nerves, following an already extensive cutting operation on the thorax and the production of a valvular lesion, was more than the animal was able to stand. It was necessary, then, to employ only the methods of abdominal compression and adrenalin injection.

If one accepts the dictum of Corrigan, that the collapsing pulse is due to the regurgitation of blood from the aorta, then any condition which retards the forward flow of blood must, of necessity, increase regurgitation, and thus render more pronounced the collapse of the pulse.

That the collapse is not increased by such a means, but entirely abolished, a glance at tracings Nos. 27 and 28 will show. They repre-

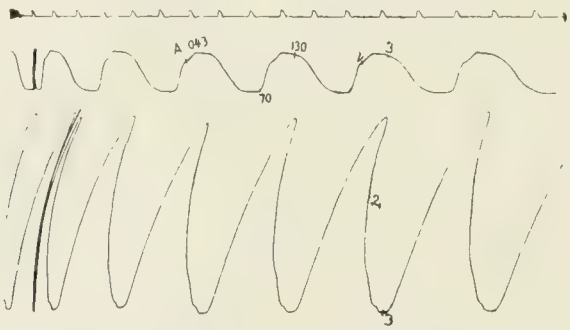

Fig. 28.—Carotid and ventricular volume curve of aortic insufficiency during compression of abdominal aorta. Note the change in the character of the pulse. A, summit of primary wave, is reached in .043 of a second after the commencement of systole. Systolic pressure, 130 mm. of Hg.; pressure at end of systole, 130 mm. of Hg.; pressure at end of diastole, 70 mm. of Hg.; systolic output, 13.5 c.c.

sent the changes in pulse form and volume curve which follow compression of the aorta at its bifurcation.

Change in the Pulse Form.—These curves show in a striking manner the truth of the statement of Marey regarding the conditions which modify the systolic portion of the pulse. There being a great disparity between the rate of inflow and the rate of outflow, the summit of the primary wave A is reached in a relatively shorter period during compression of the aorta. When the flow was unrestricted the time taken by the primary wave to attain its maximum was .065 second, while now it is reached in .043 second. The "systolic plateau," for the same reason, becomes ascending, and the dicrotic notch occupies the summit of the

curve. It will be seen to coincide exactly with the end of systole, as measured by the plethysmograph, .01 second in each.

The fall of pressure is now entirely diastolic, since the systolic plateau does not descend. The pressure which exists in the aorta at this moment is 130 mm. Hg., as contrasted with 70 mm. Hg. in the corresponding part of the ordinary curve of aortic insufficiency. There is thus established the ideal condition for regurgitation. Notwithstanding that the diastolic fall of pressure is more gradual than it is even in the normal tracing with intact valves, and only reaches the abscissa .06 second before the succeeding systole; *or,* in other words, the *conditions most favoring regurgitation caused the cessation of the collapsing quality in the pulse.*

Change in the Volume Curve.—The effect on the systolic contraction is merely an exaggeration of that which occurs in the ordinary state of insufficiency. The tension transmitted to the ventricular walls before contracting is greater, and the "loading" effect is more pronounced. The systolic contraction is still more protracted and the rate of systolic discharge slowed. It will be seen from the record that the diminished rate of output is more marked toward the end of systole, the tracing becoming more oblique as the apex is approached.

There is, however, this distinction. The tension is now so great that the tone of the ventricular wall is no longer able to counteract it, and a considerable regurgitation results. The distance from the base line at the end of diastole is shortened.

Further, so great is the resistance to be overcome in the aorta during the latter part of systole that the ventricle fails to effect so complete an emptying of its cavity. The difference in the quantity of residual blood is small, however, and does not amount to more than 2 c.c.

The record shows conclusively that regurgitation can not account for the collapsing pulse. Even with the increased systolic output and the greater pulse pressure, due to regurgitation, when the aorta is compressed, an increase of the resistance to onward flow of blood abolishes its collapsing character, and, conversely, a diminution of the resistance will exaggerate it, although this can not be tested experimentally, when the aortic valves are damaged, as the diastolic pressure is already reduced to a minimum. It is easy, however, to follow the successive changes in this type of pulse which result from the gradual relaxation of an increased resistance.

The position assumed by the dicrotic notch becomes gradually lower on the descending limbs of the pulse curve and the systolic plateau becomes first horizontal and then descending. This indicates a gradual

lowering of the pressure, which is transmitted to the ventricles at the commencement of their relaxation, since it is the pressure which exists in the aorta at the moment of closure of the aortic valves.

An increase of the rapidity of capillary escape, then, may be said to have a preservative influence on both the heart and the arterial system. It diminishes the magnitude of the pressure at the end of systole, and, therefore, prevents the transmission of high pressure to the ventricular walls during their relaxation. It also slows the rate of rise of the primary wave, and thus counteracts the tendency to dilatation of the arteries, as would be caused by the sudden stretching attending the passage of a steep wave of pressure.

The injection of adrenalin effects a change in the pulse curve which is identical with that of compression of the abdominal aorta. It raises the aortic pressure at the commencement of diastole, and, therefore, dis-

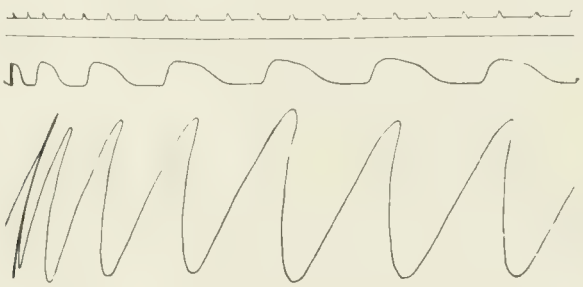

Fig. 29.—Carotid and ventricular volume curve of aortic insufficiency to show the effect of the injection of adrenalin. It is similar to that produced by compression of the abdominal aorta. Compare with the ordinary tracing of aortic insufficiency No. 27.

tends the ventricle by the regurgitation of blood. But the contraction of the peripheral arterioles retards the escape of blood through the capillaries, and the pulse ceases to be collapsing. On account of the stimulating action which it exercises on the ventricular contraction, the systole is more complete, and the effect it produces on the volume curve differs from that of abdominal compression in that the quantity of residual blood is diminished. Tracing No. 29 was taken on a fast drum when the drug had produced its maximum effect.

CLINICAL APPLICATION OF EXPERIMENTAL RESULTS.

The most important points which have been brought out from the experimental investigation of the pulse and blood pressure changes in aortic insufficiency are briefly:

1. That the so-called water-hammer pulse owes its abruptness and rapid fall not to regurgitation into the ventricle, but to an increased blood flow through the capillaries.

2. That this increased capillary flow is due, in a recent insufficiency, to reflex inhibition of the vasomotor center, probably induced by stimulation of the depressor nerve effected by the mechanical action of the pressure transmitted from the aorta.

3. This pressure simultaneously increases the ventricular tone.

4. That so long as the tonus is maintained a slowing of the pulse can not have any appreciably harmful influence on the amount of blood which regurgitates.

It becomes necessary, then, to apply these results to the aortic insufficiency which is due to disease, and to inquire as to how far they will help to explain the clinical discrepancies previously mentioned.

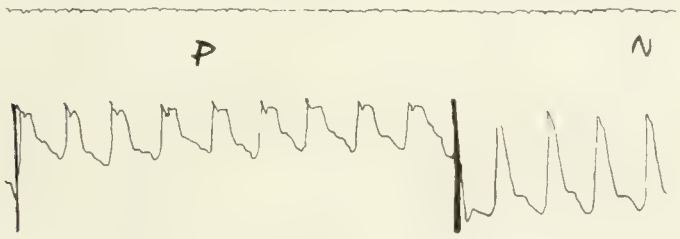

Fig. 30.—Tracing from the radial artery to show the effect of terminal constriction. P, during constriction. N, Tourniquet removed.

It is obvious that if the main fall of pressure is due to an increased rate of capillary flow it will follow that any condition which retards it should cause the disappearance of the collapse. This can readily be accomplished in the case of the radial artery by constricting the terminal vessels of the hand by the application of an elastic tourniquet. If a sphygmographic tracing be taken from a typical case of aortic insufficiency in the manner recommended by Lewis,[30] with weight instead of band fixation of the sphygmograph, the effect of decreasing the outflow from the artery will at once become apparent.

Such a tracing before and during terminal constriction is shown in Figure 30. The patient suffered from pure uncomplicated aortic insufficiency. He had a systolic blood pressure of 130 mm. Hg., and a diastolic blood pressure of 65 mm. Hg. and subjectively a typically collapsing pulse. The instrument used was a Jacquet chronosphygmograph. This instrument being a heavy one, it sufficed only to lay it over the artery

30. Jour. Physiol., Lond., 1906, xxxiv, 393.

without encircling the wrist with the usual sphygmograph band. The tourniquet was applied below the level of the thumb, well away from the sphygmograph, so that on being tightened the tracing could not be affected by the wrinkling of the skin. The contrast is striking. Before the terminal vessels are constricted the amplitude of the pulse is great, the apex of the wave pointed, and the systolic plateau is a steep decline. During constriction, on the other hand, the amplitude becomes small and the trough of the waves does not reach the abscissa, thus indicating an artery which does not empty itself. The systolic plateau is more horizontal, and the dicrotic notch assumes relatively and absolutely a higher position on the tracing. Indeed, the tracing so transformed is the counterpart in every detail of the tracings of aortic insufficiency which Sansom describes as "having a resemblance with the tracings indicating high tension."

A similar result, although in a totally different manner, has been obtained by diminishing the rapidity of capillary flow by the aid of venous constriction. As has been pointed out by Bayliss and Starling,[31]

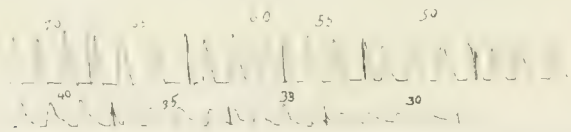

Fig. 31.—Series of tracings of the brachial artery taken with varying degrees of venous obstruction. When the pressure in the cuff is lower than the diastolic pressure the arterial inflow to the limb is not affected, while the venous return is restricted. The numbers indicate the different pressures in the cuff.

the capillary flow and pressure are greatly influenced by changes in the venous pressure, the flow being greatest when the pressure is least. If, by constricting the limb with a cuff bearing a pressure less than the diastolic blood pressure, the free inflow to the limb is not retarded, any desired amount of venous restriction may be obtained. A tracing, No. 31, from the branchial artery under such circumstances, is shown above. It will be seen that the collapse disappears and the catacrotic limb of the pulse curve becomes gradual in its fall.

So strong has been the stimulus of a dominant and preconceived idea that clinicians have sought to extend this idea into the explanation of many of the other attendant features of aortic insufficiency. Thus it is universally held that the reason why the collapse is more marked when the limb is elevated is due to the greater ease with which the blood can flow back into the ventricle. Apart from the physical impos-

31. Jour. Physiol., Lond., 1894, xvi, 157.

sibility of there being a retrograde blood current where there is a driving strength of even 50 mm. Hg., as indicated by the diastolic pressure, this view can readily be controverted by a simple experiment.

If, while the limb is elevated, the upper arm is encircled in a sphygmomanometer cuff, and the pressure raised to a point below diastolic pressure, so as to obstruct the venous return only, the intensified sensation of the collapse is now no longer felt. This experiment, while disproving the theory that the collapse is due to regurgitation, at the same time renders it evident that the elevation of the limb increases the sensation of the collapsing pulse, not by increasing backflow, but because it increases the capillary flow by hastening the venous return.

But the capillary pulsation so common in this condition is also ascribed directly to regurgitation. It is said that it is due to the empty condition of the peripheral vessels in diastole which results from regurgitation into the ventricle. In view of what has been said above, it is only necessary to quote an observation of Gibson's[32] while commenting

Fig. 32.—Apparently normal tracing from a case of aortic insufficiency which gave subjectively a collapsing pulse. The effect of an increase of systolic pressure is seen in tracing No. 34.

on this phenomenon: "It must be allowed that it may occur in conditions permitting a free passage of blood through the arterioles and capillaries into the veins." He further states that a direct venous pulse may develop in the peripheral veins, the pulsation following systole and passing from the periphery to the center.

Granted, then, that the collapsing pulse has its causation in the periphery and not in the center, the explanation of the clinical discrepancies previously mentioned becomes at once apparent. The collapsing pulse can exist only when the diastolic blood pressure is low, since when the systolic pressure remains constant the diastolic pressure is regulated by the rapidity of flow from the peripheral vessels. In other words, it is possible to receive the impression of a collapsing pulse only when the arterial walls are subjected to a slight distending force during the diastolic phase of the cardiac cycle.

32. Loc cit., p. 493.

It has, however, been frequently observed in those cases in which the diastolic pressure is low that when the systolic pressure is also low the pulse may give to the finger the impression of a sudden decline, while the sphygmograph tracing may show a more or less sustained pulse wave.

Tracing No. 32 is taken from such a case in which, with a systolic pressure of 75 mm. Hg. and a diastolic of 55 mm. Hg., the pulse felt typically collapsing. The patient, aged 20, suffered from aortic insufficiency, the result of acute rheumatism.

This discrepancy has its explanation in the fact that the pulse is not felt during the whole period of time in which the systolic wave is passing, and it is only that part of it which corresponds to the summit of the pulse wave that impresses itself on the finger. In order that a low pressure pulse, in which the pulse amplitude is small, may be palpated satisfactorily, the finger must be allowed to rest but lightly over the

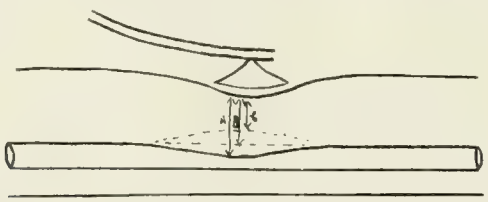

Fig. 33.—Diagram to illustrate the effect which different degrees of pressure exerted by the sphygmograph button will have on the excursion of the arterial wall during the passage of the pulse wave.

artery. There is, therefore, communicated to it only that part of the pulse which arises from the excursion of the arterial wall beyond its diastolic limit, i. e., the apex of the pulse wave. This is further evidenced by the fact long recognized by clinicians that if the wrist or forearm of a patient suffering from this disease be grasped lightly by the hand the water-hammer quality is much intensified. Under such circumstances the vessel, distended by the wave produced by the ventricular systole, is felt only at the summit of its distension. When, however, the sphygmograph records the largest amplitude of wave for a given pulse the pressure which is exerted by its pad is approximately equal to the pressure which obtains within the vessel.

During the interval between the pulse waves the arterial walls are somewhat approximated, as in Figure 33, and in this condition the systole of the ventricle will cause them to execute a greater movement. But, owing to the low diastolic pressure and to the fact that the pulse amplitude is small, the arterial wall is stretched but slightly. The arterial

recoil, therefore, will not be forcible, and it will return gradually to the position assumed during diastole.

The low systolic pressure in the patient mentioned above being an indication of a feebly contracting left ventricle, the effect of treatment was to raise it from 75 mm. Hg. to 105 mm. Hg., while the diastolic pressure remained as before, viz., 50 mm. Hg. The change resulting in the sphygmographic tracing is interesting, for it presented a fairly typical collapsing pulse, while at the same time it gave the collapsing sensation to the finger. This change in the character of the tracing can readily be explained by the greater stretching force to which the artery was subjected during the passage of the primary wave. Haycraft[33] has recently shown that within wide limits the arterial walls obey Hooke's law, which means that the amount of extension is proportional to the force which produces it. It follows, then, that the more the vessel is distended the more rapid will be the rate of recoil. It thus becomes evident how it is that the finger can always receive the sensation of a

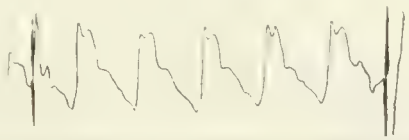

Fig. 34.—To show the effect of an increase in systolic pressure. The pulse is more collapsing.

collapsing pulse when the diastolic blood pressure is low, while it is only in those cases in which the pulse pressure is excessive that it can with certainty be recorded by the sphygmograph.

It is also easy to explain the absence of the collapsing pulse in the percentage of cases previously mentioned. These cases must have presented high diastolic pressures, although they are not recorded, since it is only within the last two years that we have been in a position to measure the diastolic pressure clinically. The high diastolic pressure in the majority of these cases was probably the result of the accompanying arteriosclerosis which most of the cases presented. It is to be noted, also, that the absence of the collapsing pulse need not be due to a small pulse pressure, i. e., the difference between systolic and diastolic pressure, or, conversely, a large pulse pressure need not necessarily be accompanied by a collapsing pulse.

A collapsing pulse can only be seen in those cases in which the diastolic blood pressure is low. The fact that a high diastolic blood pressure should cause the sphygmograph tracing to assume a gradually sloping

33. Jour. of Physiol., Lond., xxxi, 392.

line, even when there is a great range between the systolic and diastolic pressures, is due to a condition depending on the physical property of the arterial wall. Roy[34] showed that while Hooke's law is obeyed when the pressures are normal, when they are exceeded the extensibility of the artery rapidly diminishes.

From the figures given by Roy of the extensibility of the arterial walls at different pressures two pulse curves are drawn (Fig. 35).

In both instances the excess of systolic over diastolic pressure is the same, viz., 60 mm. Hg., but they differ in that the one, the diastolic pressure, is below normal, viz., 50 mm. Hg., while in the other it is somewhat above normal, viz., 80 mm. Hg. In the lower curve the amplitude is double that in the upper, the angle between the upstroke and downstroke is more acute and the dicrotic notch relatively lower. In the upper curve

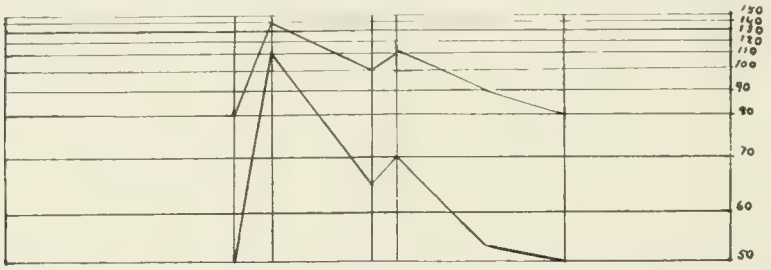

Fig. 35.—Diagrammatic representation of two pulse curves indicating the same pulse pressure, but at different diastolic pressures. The horizontal lines indicate the extensibility of the artery at given pressures (after Lewis).

upstroke and downstroke are oblique and the angle between them is widened.

In the curve taken at the low pressure there is more movement of the arterial wall for the same change of pressure. The one would be classified as a "collapsing" pulse, the other as "sustained."

THE LOW PERIPHERAL RESISTANCE IN AORTIC INSUFFICIENCY.

Starling[21] has pointed out that in disturbed conditions of the circulation the reflex mechanism called into play aims more at sparing the heart from overexertion than in counteracting the original vascular disorder. So in aortic insufficiency the function of a reflex dilatation of the peripheral vessels is a conservative one, being the method adopted by Nature to relieve the heart of the increased work thrown on it as a consequence of the transmission of pressure from aorta. This reflex action, however, is wholly distinct from that which occurs in old standing

34. Jour. of Physiol., Lond., 1881, iii, 135.

cases, which are due to disease, for now there are produced in the arterial system conditions which obviate the necessity of a continuous action on the part of the vaso-dilators.

The great changes in pressure between systole and diastole have the effect of stretching and widening the coats of the peripheral arterioles so that they remain permanently dilated. This dilation subserves the function of the reflex inhibition of the vasomotor center, which takes place after an experimental insufficiency. It was shown by Romberg and Hasenfeld[10] that several months after an insufficiency had been produced in rabbits the vasomotor nerves were less active than normal and the same degree of peripheral constriction could not be effected by their stimulation.

The question, then, immediately arises why the ventricle becomes hypertrophied and dilated to such an extraordinary extent, if an appreciable quantity of blood does not regurgitate, and the increased work thrown on the heart can be greatly obviated by a peripheral dilatation.

In order to make the point clear, certain properties of the contractility of muscle must be mentioned briefly. Haidenhain[35] has shown that when the tension on a skeletal muscle is increased before it contracts, the energy of the contraction becomes greatly augmented. The apex of a frog's heart ceases to beat under ordinary circumstances, but it can be made to contract by distending the cavity of the ventricle with fluid. Gaskell[36] also showed that after the apex of the frog's heart is rendered quiescent by crushing a ring of tissue above it, it can be made to contract again by clamping the aorta.

The excitory effect of increased tension in both cardiac and skeletal muscle is thus firmly established. Moreover, this mechanical effect involves a great expenditure of cardiac energy, for it is accompanied by an augmentation of all the chemical processes which accompany contraction, as is evidenced by the increase in heat production. In aortic insufficiency, instead of a pressure equal only to the atmospheric pressure as in the normal ventricle, the intraventricular pressure tracings show that there is a pressure on the ventricular walls during diastole, equal to the diastolic pressure in the aorta. The ventricle is thus locally stimulated to increased exertion and its contraction becomes similar to that in which a muscle is extended before it contracts. So long as the heart is able to supply the increased demands thus made on its energy there may neither be hypertrophy nor dilatation, and we have the authority of Krehl[37] that every case of aortic insufficiency is not accompanied

35. Quot. by Gaskell, Shaefer's Text-book of Physiol.
36. Schaefer's Physiol., vol. ii, 170.
37. Clin. Path., trans. Hewlett, p. 38.

by an enlargement of the left ventricle. When, however, the cardiac muscle becomes inefficient it will give way to the stretching influences which bear on it during diastole, and the cavity of the ventricle will enlarge. This is immediately followed by hypertrophy. But in so doing the increased work which the heart now accomplishes, as a consequence of the greater systolic output, has the effect of raising the mean pressure in the arterial system. There is thus established a condition in which there is a greater transmission of pressure and a still greater expenditure of energy. The condition is a progressive one, for the greater the hypertrophy and dilatation the greater the transmission of pressure and consequently a greater waste of cardiac energy.

It is thus evident how potent a factor is a low peripheral resistance in the preservation of the heart in aortic insufficiency. It not only lessens the tendency toward the regurgitation of blood, but it also reduces

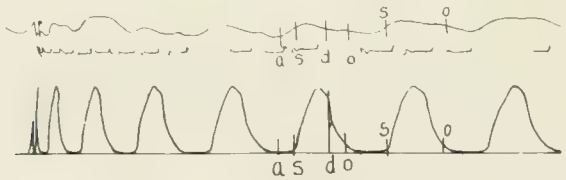

Fig. 36.—Simultaneous tracing from the left auricle and the left ventricle after the production of aortic insufficiency. a, auricular systole; s, ventricular systole; d, ventricular relaxation; o, opening of the mitral valves. There is a fall in the auricular pressure during the contraction of the ventricle. The valves must, therefore, be competent.

the influence of the increased tension on the ventricle as a stimulating agent.

It may not be out of place to mention here the frequency with which a transient mitral insufficiency may develop in the course of an experiment in which the aortic valves have been damaged.

A simultaneous tracing of the intraauricular and intraventricular pressures gives a ready means of detecting such incompetency of the mitral valves, for instead of the normal fall in pressure, which occurs in the auricle during ventricular systole, there is a systolic rise of pressure when an insufficiency develops. Such is seen to take place in tracings Nos. 36, 37 and 38. These three tracings were taken at different times during the course of one experiment.

In No. 36, there being a fall of pressure in the auricle during the contraction of the ventricle, s-d, the mitral valves are competent. In No. 37 there is a systolic rise of pressure, which is to be interpreted as indicating an inadequate closure of the auriculo-ventricular orifice.

Tracing No. 38 was taken an hour later, and it shows that the ventricle has recovered, for there is now a systolic fall in pressure in the auricles.

This effect is probably due to periodic changes in the ventricular tonus, which, when lowered, permits of ventricular dilatation, and this is followed by a relative insufficiency at the mitral opening. This view is supported by the result obtained by stimulating the peripheral end of the vagus, which produces a marked diminution in the ventricular tone.

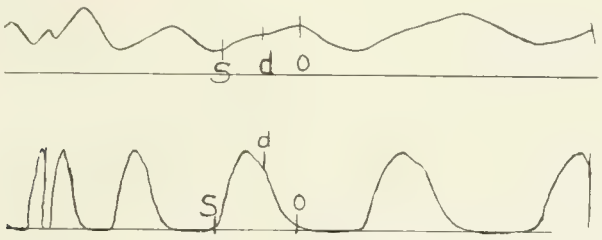

Fig. 37.—Same as No. 36, but there is a rise in auricular pressure during the contraction of the ventricle, s-d. The valves are incompetent.

Tracing No. 39 shows the effect of such stimulation. It will be seen that immediately before stimulation the ventricular systole, s-d, is accompanied by a slight fall in auricular pressure (the valves are competent), while during stimulation there is a marked rise in pressure (an insufficiency has developed). O marks the commencement of the fall of auricular pressure and, therefore, the time of opening of the mitral valves.

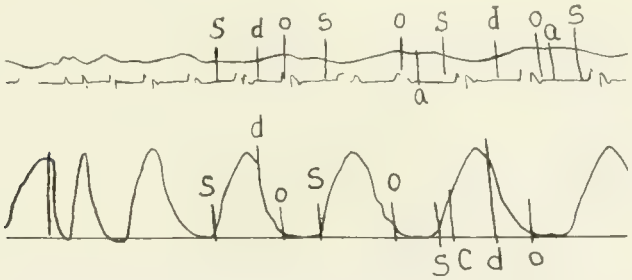

Fig. 38.—Same as No. 37, one hour later. The mitral insufficiency is no longer present, for now the pressure in the auricle falls during ventricular systole, s-d. Lettering as above.

It is clear that the production of a relative insufficiency at the mitral orifice, in addition to an aortic lesion, may, to a great extent, be avoided by lowering the diastolic blood pressure. For, when the diastolic pressure is sufficiently low, the ventricular tone is able to overcome it and no dilatation results.

The conclusion, then, which is to be drawn from the experimental and clinical study of this disease is that the condition which is most favorable in a patient suffering from aortic insufficiency is a low diastolic blood pressure. This is supported by the fact, long recognized by clinicians, that the outlook in a case of aortic insufficiency resulting from rheumatic endocarditis is more favorable than one in which the lesion has been the result of arteriosclerosis (Osler[38]). The reason is sufficiently obvious, for in the former the diastolic pressure is low, while in the latter, as a consequence of the rigid arteries, the diastolic blood pressure is high.

Finally, this is not without a bearing on the question of the use of digitalis in this disease. It has been contended that this drug is contraindicated because by prolonging ventricular diastole it favors increased

Fig. 39.—Simultaneous tracing from the left auricle and left ventricle after production of aortic insufficiency to show the effect of vagal stimulation. The diminution in tone causes a dilatation of the ventricle and a relative insufficiency at the mitral orifice. Before stimulation the pressure in the auricle falls during the ventricular systole, while during stimulation there is a rise of pressure from s-d.

regurgitation. But it has been proved already that a mere lengthening of the period of diastasis is not harmful, if there be no diminution of the ventricular tone, since the pressures in the ventricle and aorta are equalized as soon as the ventricular filling is completed. The harmful influence of digitalis can not result from its action in slowing the heart rate. It is due to the action which the drug possesses on the peripheral arterioles. As is well known, it has a powerful constricting action on these vessels, and thus, by raising the diastolic pressure, is its effect deleterious. Theoretically, strophanthus should be a more useful drug, since, as shown by Fraser,[39] it does not possess this constricting quality to the same degree.

38. Princ. and Pract. of Med., 1898, p. 517.

39. Action and Uses of Digitalis and Its Substitutes, with Special Reference to Strophanthus. Read before Brit. Med. Assoc., Cardiff, 1885, p. 15.

SUMMARY OF CHIEF CONCLUSIONS.

1. The work of Henderson is confirmed in that the cardiac cycle is not diphasic but triphasic, and consists of systole, the period of the ventricular discharge; diastole, the period of ventricular relaxation and filling; diastasis, the period of rest.

2. The effect of the production of aortic insufficiency in the dog is to increase the amount of systolic output by only a fraction of a cubic centimeter of blood.

3. The volume of blood which regurgitates is negligible.

4. The transmission of pressure to the ventricle increases the ventricular tonus.

5. It also produces a reflex inhibition of the vasomotor center.

6. The fall of pressure in aortic insufficiency is due to the diminished peripheral resistance thus induced, and is not caused by loss of blood from regurgitation.

7. The increase of pulse pressure—the difference between maximum and minimum pressure—is due to a lowering of the diastolic pressure. There is no increase in the systolic pressure.

8. The main fall in pressure is systolic in time and is due to an increased blood flow through the capillaries.

9. So long as the tonus of the ventricle is maintained, a slowing of the heart rate does not favor increased regurgitation.

Johns Hopkins Hospital.

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